

Social Irresponsibility in Science

THE British Society for Social Responsibility in Science is perhaps more than other new organization in great need of that claim on public attention which the Americans call credibility. Everybody agrees, of course, that no harm can be done by a sober examination of some of the questions that sensible people must ask about some of the social problems occasioned by modern science and, more particularly, by modern technology. There is even a need that public attention should be drawn to some of these issues and to the general need for vigilance. In this sense, the British Society for Social Responsibility seemed to have a useful job to do when it began just over two years ago. Its difficulties since then seem to have stemmed largely from the problem of how to provide a commentary on current affairs which is at once lively and balanced.

The society's efforts so far have not been conspicuously successful. What might have been a valuable public discussion on the ethical problems of modern biology (see *Nature*, 228, 900; 1970) seems to have tailed off into discussion of the process of radicalization of science and even some of the familiar problems of Vietnam. It is of course unavoidable that an organization like this should be seen as a vehicle for other causes than those included in the prospectus and in ordinary circumstances many scientists would be willing to forgive the society its errors of judgment and its excesses for the sake of what might be done.

It is therefore a great misfortune that the society should now have chosen to make an ass of itself in public over its relations—and in particular its lack of a formal relationship—with the British Association. At the last annual meeting of the British Association in Durham, members of the society created a stir, sometimes a healthy stir, by speaking up at public meetings, sometimes by interrupting public meetings and by organizing public spectacles of various kinds.

Since then the society has been debating within itself the principles on which its relations with the British Association should be determined and the outcome seems to be the decision not for the time being to cooperate with the association. This view is summarized in the current issue of *New Scientist* (February 11, 1971) by Mrs Hilary Rose, the new chairman of the society, who protests (quite legitimately) at the composition of the review committee trying to hammer out a role for the association in the years ahead (see *Nature*, 228, 697; 1970) and then goes on to say that the society

"would gladly cooperate with a rejuvenated BA to tackle the problems of the mutual impact of science and society. However, a virtual revolution in BA attitudes and practice is required. Without some concrete evidence that the BA at least realizes the magnitude of the task it faces, BSSRS will feel such cooperation to be futile. It would merely feed complacency, and weaken the impulse to reform."

As a part of the same solemn movement of protest, Dr J. R. Ravetz, one of the council of the British Society for Social Responsibility in Science, has taken the deliberate and weighty step of resigning from the association's innocent committee responsible for conducting the

affairs of Section X. On the face of things at least, it looks as if diplomatic relations between the two bodies have been severed with all the pomp and dignity appropriate to political rows between the smaller sovereign states.

In all this, it is a great misfortune that the British Society for Social Responsibility in Science has so quickly given in to the temptation to pomposity which has so often in the past been one of the most serious deficiencies of the British Association. The truth is that a body which sets out to be an enlightened pressure group cannot safely afford the luxury of haughtiness. If Mrs Rose means what she says about the society's willingness to cooperate with a rejuvenated British Association, is it not a part of her colleagues' job to help to see that something they would welcome does actually emerge from the deliberations of the review committee, and from the decisions that will eventually be taken about the reorganization of the British Association? If, on the other hand, the British Society for Social Responsibility in Science considers that it would itself be able to perform the contemporary work that the British Association could (and should) be doing, would it not be much more honest to say just that? And would it not then be proper for the society to show that on some occasions at least it can provide the world not merely with the definitions of problems which it considers to be important but also, now and again, with some attempts at constructive solutions? With so much talk and so little work to show, the society has unknowingly as serious a problem on its hands as the British Association.

Postal Strike

THIS issue of *Nature* will be the first to be distributed outside North America and parts of the United Kingdom since the beginning of the British postal strike on January 20. Missing copies will be despatched as soon as the strike is over but there will unfortunately be some delay.

Until further notice, and certainly for some days after the strike is over, contributors and subscribers outside Britain should write only to the North American office of *Nature*, 711 National Press Building, Washington, DC 20004 (telephone 202 737 2355). Communications by telex may be sent either to Washington (64280) or to London (262024).

Manuscripts for publication which may eventually be accepted but which are at present embedded in the British postal system will not have been acknowledged as received, and authors wishing to ensure safe delivery should send a duplicate (so marked) to Washington.

Potential contributors may wish to know that the incoming flow of manuscripts for *Nature* has been so reduced by the strike that the time spent on handling and assessment is much reduced. In the physical sciences in particular, publication is now extremely rapid.



The Great Greenhouse Scare

THE belief that the civilized world will one day be washed away by the increase of sea level that might result from the melting of the Antarctic ice which in turn might be accomplished by the accumulation of carbon dioxide in the atmosphere has been for some years the popular and frightening legend much quoted by public speakers, politicians and professional doomsday men. And the tales of impending doom have often been so vivid that many innocent souls must have found it hard to look at the sea without fearing engulfment. The culprit, of course, is the burning of fossil fuel, for decades now one of the raw materials of industrial society, so that the threat posed by the presence of carbon dioxide in the atmosphere has been for many people yet another stick with which to beat technology. In the circumstances, it is valuable that the MIT Press has now published the report of a study group which met at Williams, Massachusetts, last summer under the title of the 1970 Study of Critical Environmental Problems. Among other things, this careful study shows that the greenhouse effect, as it is called, has been a greatly exaggerated topic for anxiety.

There seems to be no doubt that the concentration of carbon dioxide in the atmosphere is increasing steadily—measurements at several sites suggest that in the past decade carbon dioxide concentration has increased by 0.2 per cent a year to about 320 parts per million. The amount of carbon dioxide released each year into the atmosphere is a simple function of the amount of fossil fuel burned, at present rather more than 10^{10} tonnes a year. The atmospheric reservoir of carbon dioxide appears to be about 2.5×10^{12} tonnes, so that the annual increment of carbon dioxide to the atmosphere is a substantial fraction of one per cent.

One interesting question is to know what happens to this carbon dioxide. The atmosphere is linked with two other reservoirs of carbon—the biosphere and the upper layers of the oceans. The authors of the report guess that the stock of carbon in the biosphere is comparable in size with that in the atmosphere but probably larger, and that the effective size of the oceanic reservoir depends crucially on the time scale considered to be relevant—the carbon in the first 100 metres or so of sea with which atmospheric change is comparatively rapid should be between a fifth and a half of the atmospheric reservoir, but the first kilometre would include a very much larger amount of carbon dioxide.

In these circumstances, it is not surprising that roughly

half of the annual addition of carbon dioxide to the atmosphere disappears. In an entirely natural world, no doubt, one consequence of adding carbon dioxide to the atmosphere by the exhausts from fossil fuel chimneys would be to increase the growth of plant life. This, in practice, is now a matter on which agriculturists have as much to say as the persistent burners of fossil fuel, and one valuable service provided by the Williams study is that it shows how pronounced changes in the pattern of agriculture—the removal of the great tropical forests, for example—could have as marked an effect on the atmospheric reservoir of carbon dioxide as the past decade's consumption of fossil fuel. For both reservoirs, however, it is now clear that the processes of exchange between the atmosphere and the other reservoirs are at least sufficiently rapid to ensure that additions to the atmosphere are not permanent, which means that if the worst came to the worst and there were signs that carbon dioxide concentrations in the atmosphere were becoming large enough to bring about a change of temperature comparable with the natural fluctuation from one decade to another, it would be feasible to undo the damage simply by calling a halt to the rate at which fossil fuels are consumed.

What of the effects of carbon dioxide once in the atmosphere? What emerges most clearly from the study group's report is that the predictions of the simple greenhouse effect are an upper limit. With reasonable assumptions about the continued consumption of fossil fuel, the study group suggests that there may be an increase of 18 per cent in the concentration of atmospheric carbon dioxide by the year 2000, and the simple consequence of this in an entirely static atmosphere would be to increase the temperature of the surface of the Earth by about 0.5 degrees and to decrease the temperature of the stratosphere above 20 kilometres by about one degree. The snag here is that these calculations leave entirely out of account the way in which increased heat energy near the surface of the Earth would tend quickly to be dissipated by meteorological processes of various kinds. At the very least, there would be increased evaporation and, at the same time, increased absorption of carbon dioxide by the oceans. But quite a lot of energy would also be carried higher into the atmosphere by cyclonic processes. In short, half a degree by the end of the century (by which time nuclear power should have taken the load off the fossil fuels) is much more than sober men should worry about.

Who would Live in California?

THE most remarkable feature of last week's earthquake in California (see page 520) is that an event which rates merely 6.5 on the Richter scale, and which causes fewer than a hundred people to die, should attract such attention. After all, the Los Angeles earthquake is not the first serious event of its kind to have occurred this year. On this occasion, the Italians have a doubtful pride of place with an earthquake just north of Rome. And the past few years have seen much more spectacular and damaging events in Iran, Turkey, North Africa, Yugoslavia, the

Philippines and Chile. On the average, earthquakes such as that in Los Angeles last week occur about a hundred times a year in various places in the world. The records show that on the average there should be about twenty earthquakes of magnitude 7.0 or greater in a year. In these circumstances, the only explanation for the interest which the Californian earthquake has excited is that it has occurred in one of the few nations in which communications of all kinds are so good that the disaster can be described almost as it happens, not merely when rescue

teams have been able to thread their way over broken ground days afterwards. But an earthquake in California is also remarkable because it is a reminder that those who live there do so in the knowledge that earthquakes are a part of Californian life. Is it courage or foolhardiness that makes people live there in ever-increasing numbers?

By now, the properties of the San Andreas fault system are quite well described. Measurements in the past decade have shown that on those sections of the fault where movement is comparatively uninhibited, the annual displacement may be as much as three centimetres a year. Where the fault runs out to sea, in the southern suburbs of San Francisco, however, the fault appears to be locked as it is in the more complicated region to the south, around Los Angeles. But it has also become clear in the past two years or so that the scale of the tectonic movements responsible for the movement along the San Andreas fault is so great that the movement is bound to be as persistent as any geological process. Briefly, two tectonic plates are moving relative to each other and the fault system in California is merely a consequence of that. If anything, the development of plate tectonics should have sharpened the anxieties of those in California who fear that it can be only a matter of time before there is a much larger disaster than last week's comparatively small earthquake caused.

The first thing to be said is that the system of faults in California is so complicated, and the coastal strip is for much of its length so narrow, that there is very little hope of avoiding trouble by siting buildings away from the immediate locality of known faults. In any case, the damaging effects of a large earthquake reach several miles out from the source of trouble. It is true that mountain sites are probably safer than those in valleys or on the flat, but the extent to which a building will be shaken by a serious disturbance probably depends much more on a detailed relationship of the foundations of a building and their substratum than on any simple rule of thumb. According to Dr Charles Richter, there have been three earthquakes in California of magnitude greater than eight in the past century, one of them the San Francisco earthquake of 1906. Earthquakes of magnitude greater than seven are more frequent, perhaps four a century, but earthquakes of magnitude six, which are quite large enough to cause great damage in a city which is sufficiently near by, occur in California on an average once a year. Evidently there are few places reasonably close to the fault system at which the risk of earthquake damage can be considered small. In fifty years, four of the magnitude six earthquakes have occurred in circumstances as damaging as that last week, a frequency of roughly eight per cent. Would it therefore be reasonable to suppose that there will be a repetition of last week's trouble every twelve years on the average, an earthquake of magnitude seven near some important town every century or so and an earthquake of magnitude eight damaging a region up to a hundred miles across every two centuries or so? Or would it be prudent to suppose that the pattern of the past, with damaging earthquakes in southern California (1857) and San Francisco (1906) will be repeated at some point in the years ahead? These are questions for gamblers to attempt to answer. Whatever the truth, and given the way in which the continuing development of California implies that each year the risk that an earthquake will be near an important centre is increased as is the density with which dollars are invested in bricks and mortar, the average

anticipated cost of earthquakes in California must amount to several hundred million dollars a year, the equivalent of a tax of, say, \$25 per head per year for California as a whole.

Merely to make this kind of calculation, full of speculation as it is, is a powerful reminder of the scale on which California should be planning for its uncertain future. Although there may yet be developed means of warning people of immediately impending trouble, there is no chance that earthquake prediction will ever be married to regional planning with such delicacy that people will know where not to build towns and factories. The best that can be hoped for is advice for evacuating them in time. It is also improbable that some of the techniques being talked of for relieving pent-up stresses in association with fault systems will be able, if ever successful, to avert any but the obvious dangers. In the circumstances, what California needs most urgently is not so much research on earthquake mechanisms, important though that may be, but a well-run state-wide insurance programme which will allow the frontiersmen of California to pay for the cost of earthquake disasters year by year, not only when disaster strikes. There is no reason why those living in California now should evacuate it, but is there not a case for thinking that those about to move there to build factories should think of going elsewhere?

100 Years Ago



THE MICROSCOPE

IMPROVEMENTS IN THE LENSES OF MICROSCOPES

FOR some time, people in England have been content to let the improvement of the optical powers of the microscope remain entirely in the hands of the makers, believing, apparently, that Mr. Lister had effected all in his suggestions and improvements that could be desired. Dr. Royston Pigott, an able mathematician, formerly Fellow of St. Peter's College, Cambridge, and a Doctor of Medicine of that University, was not, however, inclined to look at the matter in this way, and for many years has been working and experimenting with a view, first, to test the accuracy of our best object-glasses, and, secondly, to suggest means for their improvement. It should be remembered that Oberhauser, Nachet, and especially Hartnack, on the Continent, not satisfied with the old system of combinations for object-glasses, and not having the benefit of Lister's researches, have made excellent objectives on a totally different system, and during the last few years the last-named maker has carried his system of "immersion lenses" to such a point of excellence as, really to surpass the best glasses on Lister's system, in definition, penetration, working distance, and illumination. Those who do not admit the excellence of these objectives, which are now used by nearly all German histologists, have probably seen older glasses, made at a time when Hartnack had not reached his best. It is worth stating, now that the Parisian opticians are inaccessible, that Gundlach of Berlin has succeeded in making excellent glasses of high power at astonishingly small prices, some of his 1-12ths and 1-16ths immersion 1-16ths (so-called), being admirable in their performance. They are not, however, equal to Hartnack's glasses, which, though costing far less than what similar English glasses cost, yet are more expensive than Gundlach's. It is only fair to all parties concerned to state that the terms 1-8th, 1-12th, 1-16th, &c., as now applied to an object-glass, appear to have no definite meaning, but depend on the caprice of the maker, since the magnifying power of glasses, with the same fraction assigned to them, differs enormously.

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OLD WORLD

COMPUTERS

More Favours for ICL?

IN its year-old examination of the British computer industry, bisected by the general election, the House of Commons Select Committee on Science and Technology is once again taking evidence from government departments. Judging by last week's session with representatives of the Department of Trade and Industry, much of the evidence taken before the election should still be relevant. According to Dr I. Maddock, Controller of Industrial Technology in the department, there has been no significant reorganization of the divisions of the department that deal with computers and electronics, no significant change in their staffing, and no change in the relationship of the department with the Ministry of Defence, the Atomic Energy Authority, and the Civil Service Department. But a review is under way of the manner in which computers are bought for government departments, and a ministerial announcement is "not many weeks away".

Much of the discussion revolved around the amount of research and development that the British computer industry needs to do in order to sustain itself, a theme which the committee continually returned to last year. Dr Maddock reckoned that an expenditure of £15-20 million for several years would be needed to bring a family of computers into the market place, but Mr Ian Lloyd, a member of the sub-committee, thought this a serious underestimate bearing in mind that the 360 series cost IBM \$3-4 thousand million. Dr Maddock's reply was that this sum included leasing finance, software and so on, and that £1 buys more R & D work in Britain than does \$2.4 in the United States.

Including payments to ICL under the merger agreement, the total amount of R & D work sponsored by the government through the Department of Trade and Industry was £17 million last year and £16.1 million this year. During the period 1964/65 to 1969/70, SRC research grants in the same area came to £2.8 million. It is difficult to say how much the British computer industry itself is spending on R & D, chiefly because a large part of it is American-owned and to some extent living off research in the United States and because the industry also benefits from research in electronics, but Dr Maddock put last year's expenditure at £20-25 million. The new government has agreed to fulfil its obligations under the merger agreement with ICL, but there has been no discussion about future payments after the last payment under the agreement of £2,250,000 which is due in April.

It was clear that Dr Maddock would like to see the government give greater preference to British computers in its purchases, although he pointed out that it is frequently difficult in this context to say what is "British" and what is not. Sometimes it is necessary to examine individually each model that a firm produces to discover the extent to which it contains British components, and in central government a computer is defined as British if fifty per cent by value is British. Dr Maddock's personal opinion was that there should be what he called a "Buy British Act" along the lines of the "Buy American Act" which operates in the US Department of Defense and has given a boost to American producers. Indigenous software should also be preferentially treated, in so far as this could be done.

Towards the end of the session the committee steered the questioning toward the problems of the National Computing Centre, which was examined the previous week (*Nature*, 229, 444; 1971). Dr Maddock talked of a change of tempo in the affairs of the centre; the department is speeding up the rate at which the centre is moving towards self-support. One of Dr Maddock's colleagues, Mr J. W. Nicholls, said this desire of the department was reflected in the reduction in the grant-in-aid which the centre will receive next year. But Dr John Cunningham, a member of the committee, referred to the view in the computer industry that the National Computing Centre should restrict itself to non-profit-making activities, and wondered how this could be reconciled with the department's aims for the centre. Mr Nicholls thought that ways could be found for funding specific projects that were in the national interest, and that the centre could earn money by giving advice to foreign governments. As a member of the council of the centre, Mr Nicholls said that he intends to see it slimmed down, but he was in favour of keeping the centre and of pushing it towards Europe.

POPULATION

Gloom in the Lords

GLOOM, mixed with occasional optimism, filled the chamber of the House of Lords last week during a wide-ranging debate on the growth in world population. Lord Snow, who initiated the debate, said he believes that "the future is black", chiefly because mankind is too concerned with parochial problems to devote enough attention to important issues which face the world. On the side of the optimists, however, Lord Blackett confessed that he is like the would-be eighteenth century philosopher who tried to learn philosophy but gave it up,

because "cheerfulness keeps breaking in".

The gloom was cast by the figures given by Lord Snow when he opened the debate. The world population had reached 1,000 million by 1830, and it increased to 2,000 million by 1930. Between 1930 and 1960, another 1,000 million people were added, and by now the world population has probably reached 3,500 million. At the end of the century, the figure will be near 7,000 million and, according to Lord Snow, unless action is soon taken, there will be 14,000 million people on the Earth early in the next century. "These are terrifying figures," Lord Snow said, and he laid much of the blame for the situation at the door of medical technology. This technology, he suggested, had spread throughout the world faster than any other so that infantile mortality in any part of the world—poor or rich—was greatly reduced. "Technology, remember, is a queer thing," he said; "it brings you gifts with one hand and it stabs you in the back with the other."

But the answer, of course, is not to restrain medical technology, but to get to grips with the consequences. Unfortunately, however, Lord Snow had few suggestions to offer—"all the steps that one can suggest seem quite minor judged by the cataclysmic size of the whole position, the whole developing crisis". The notion that the problem of feeding such a huge population will be overcome by human ingenuity is false optimism gone mad, Lord Snow said, but nevertheless he had much to say in favour of the so-called "green revolution" and would like to see an infrastructure developed to keep the advances in crop control made in the past decade going. This meant putting more money into the activities of the World Bank and the agencies of the United Nations.

But what the problem really boiled down to is the Matthew effect—to them that hath shall be given—and Lord Snow suggested that the gap between rich and poor nations will widen unless the poorer countries can be persuaded to work from within to reduce their own rate of growth. Lord Snow's pessimism springs chiefly from the fact that he can see no real way that this can be done, and the only ray of hope that he offered is that young people are "extremely sensitive to the problem".

Society, said Lord Blackett, had thirty years in which to change its fundamental assumptions about population, and he was much less pessimistic about the prospects. "I have an irrational hunch that we are not going to destroy ourselves over this issue," he said, and he obviously took some heart from the experience of Yugoslavia, Hungary and Japan, all of which have got their birthrates down to a stable level. Lord Blackett was sure that the world could easily accommodate 7,000

million people—indeed, he could see no way in which the predicted increase during the next 30 years could be curtailed—and population policies should be aimed at securing a stable population by about half way through the next century. As a start to achieving a stable population in the world, Lord Blackett suggested that Britain should seriously consider the consequences of adopting a population policy.



Lord Blackett: "Cheerfulness keeps breaking in."

Other speakers in the debate also toyed with the idea of instituting a population policy in Britain, and this has also occupied the Select Committee on Science and Technology during the past session. But the chief problem still remains how to influence the population of the developing countries. As Lord Blackett suggested, much more thought and research into the problem are needed, but in the meantime an announcement by Baroness Tweedsmuir of Belhelvie that the government is increasing its contribution to overseas aid, to the IPPF and other agencies concerned with population studies, is welcome news indeed.

TECHNOLOGICAL FORECASTING

What Went Wrong?

THE financial floundering of Rolls-Royce and the huge cost escalations of the Concorde project are the product of essentially the same shortcoming—a grave underestimate of the costs of new technology. The Social Science Research Council has therefore acted with a fine sense of timing in announcing that it is to give a grant of £75,000 to the Science Policy Research Unit of the University of Sussex for research into forecasting techniques. The research will be essentially a series of case studies of technological projects which have greatly exceeded their cost forecasts.

The research group involved in the study will be a mixture of social scientists and natural scientists, and the ultimate goal will be to produce a forecasting tool which eliminates the almost inevitable bias towards underestimating costs that is evident in much technological forecasting. The first step will be to determine what has caused this underestimation, and this will involve separating the deliberate bias from the accidental bias. The SSRC believes, for example, that underestimation of costs may be due in part to "a fundamental conflict of interest between scientists and engineers on the one hand, and managers and accountants on the other"—engineers may deliberately underestimate the difficulties in order to get a project accepted by the board of directors.

Having separated the deliberate from the accidental bias, the Science Policy Research Unit intends to use the findings to develop a technique for technology assessment which also includes provision for social effects of new technology. This involves an analysis of the effect on social attitudes of the failure of technology to live up to the promises that are made on its behalf by the forecasters.

CHEMICALS

BP in Trouble too

INFLATION seems to be overtaking the chemical companies one by one. Less than a month ago Shell Chemicals announced a "reappraisal" of its huge expansion at Carrington and Stanlow (see *Nature*, 229, 291; 1971) and now BP Chemicals International has announced the cancellation of a benzene project at Grangemouth which was to have cost more than £1 million, and the rephasing of the construction of a chemical plant at Baglan Bay, South Wales.

Most of the plans for the Baglan Bay project were completed at the end of 1968 but the total cost has now escalated by about 20 per cent to £100 million. It seems, however, that only one or two of the later plants within the complex will be affected. BP Chemicals is planning a purge on operating costs to try to combat the effects of inflation and the inevitable targets are the wages and salaries bill, and research and development. The company believes, however, that it will be able to streamline its research and development effort so that it will cost less but produce the same results.

At the end of last year, the parent company, British Petroleum, was obliged to arrange short term credit amounting to about £100 million because of difficulties in the tanker charter market; this fact and the last set of quarterly results only serve to emphasize the difficult period which BP and the rest of the chemical industry are going through.

CANCER RESEARCH

ICRF Expands

THE Imperial Cancer Research Fund (ICRF) last week announced the establishment of two more research units, a medical oncology unit which will be accommodated at St Bartholomew's Hospital, and a tumour immunology unit, eventually to be housed in new buildings at University College, London. It seems likely that research in the new units will begin in October this year.

The establishment of these extra-mural units is a clear departure from the Fund's previous research policy; in the past, the ICRF has supported research into cancer chiefly through work carried out in the Fund's own laboratories at Lincoln's Inn Fields and at Mill Hill. As the demand for space at these sites has intensified, however, it has become necessary to find other ways of housing specialized and important research projects. The first indication of this fresh approach was the establishment of the breast cancer research unit at the New Cross Hospital in 1969. The new units, however, are evidence not only of expansion in terms of space, but also in terms of cooperative research.

St Bartholomew's Hospital will provide accommodation and hospital facilities for the medical oncology unit, but the ICRF will pay the running costs, which have been estimated at £250,000 over five years. An important feature of this unit will be the connexion which can be established through the director, Dr G. Hamilton Fairley, between the unit and the Chester Beatty Research Institute, where Dr Hamilton Fairley will continue his research on a part-time basis. The eventual scheme is for links to be forged between the ICRF, the Chester Beatty, St Bartholomew's Hospital and a large regional hospital. Such cooperation should lead to unique opportunities for clinical cancer research. Dr Hamilton Fairley regards the unit as the clinical arm of the ICRF; he is particularly anxious that the plan should make it possible for cancer patients to be treated at the unit before they have received any other treatment which could complicate their symptoms.

The ICRF is providing about £82,000 to cover the cost of building and fitting out the tumour immunology unit at University College, and a further £300,000 will be found over five years to pay the running costs. The total financial commitment for the first five years that the two units will be in existence is therefore just over £0.5 millions. Finance will be provided chiefly from the ICRF's annual income, but there is a substantial reserve fund available to cover inflation.

The tumour immunology unit will be run by Professor N. A. Mitchison, and recruitment of research staff has already begun.

NUCLEAR POWER

Rethinking at BNDC

THE Nuclear Power Group, one of the two consortia set up during the reorganization of the British nuclear power industry in the late 1960s, seems to be losing the competition of its twin, British Nuclear Design and Construction Ltd, in the field of steam generating heavy water reactors (SGHWR).

Although BNDC says that development work on the SGHWR will be continued, it certainly seems that the consortium's prices are not as competitive as those of the Nuclear Power Group. The NPG is, for example, very hopeful of winning the contract for the Jervis Bay project in Australia whereas the BNDC tender was not even shortlisted. Another clue to the changing attitude of BNDC towards the steam generating reactor is the consortium's decision not to compete for the Stakeness reactor contract offered by the North of Scotland Hydroelectric Board. The NPG, however, regards the Stakeness contract as vitally important because it marks the first expression of real commercial interest in the SGHWRs within the UK.

The Nuclear Power Group is also confident that the SGHWR is a particularly good export proposition because it does not require the large and sophisticated high pressure boilers which are necessary in pressurized water and boiling water reactors. The group says that as much as 85 per cent of a typical SGHWR can be constructed within the purchasing country, even if that country is not particularly advanced technologically. The design of steam generating reactors is also very flexible and higher outputs can be achieved simply by adding extra light-water tubes rather than by carrying out fundamental boiler design changes.

The decline of SGHWR impetus within BNDC may also reflect some rethinking within the GEC-English Electric-AEI group which owns 25 per cent of the consortium. The GEC group is known to be pursuing an internal policy of reducing the number of designs across its whole range of power engineering products in an effort to reduce costs and increase reliability. It is also significant that the GEC group is taking an active interest in a Westinghouse design for a pressurized water reactor and is involved with Westinghouse in a £60 million contract for such a reactor in South Korea.

Parliament in Britain

Swann Report

MR JAMES PRIOR, Minister of Agriculture, said that the government intends soon to implement many of the recommendations contained in the Swann Report on the use of antibiotics in medicine. The retail sale of feeding stuffs containing certain antibiotics will be made unlawful except on prescription, to prevent antibiotic-resistant strains of bacteria being passed from animals to humans. From March 1, 1971, penicillin, chlortetracycline and oxytetracycline will be restricted, and from September 1, 1971, tylosin, sulphonamide drugs and four nitrofurans will be brought under the regulations.

Mr Prior also announced that some drugs will be derestricted next year. (Written answers, February 11.)

Research Expenditure

THE research associations governed by the Department of Trade and Industry have been deriving a steadily growing proportion of their income from contract research during the past five years. Sir John Eden, Minister for Industry, said that the value of such work carried out by the associations in 1964 amounted to £799,516, but in 1969 it had reached £1,944,394. These totals represent 8.7 per cent and 13.5 per cent of the total gross income of all the Department of Trade and Industry in 1964 and 1969 respectively.

In reply to a later question, also from Mr John Osborn, Mrs Thatcher, Secretary of State for Education and Science, said that in 1968-69 payments for research services and other appropriations in aid contributed about £3 million—less than 10 per cent—to the expenditure by research council establishments and research expenditure by the Natural History Museum. Public corporations and private industry provided £4.1 million for research in universities. This amounts to about 4.6 per cent of the universities' expenditure on research and development in that year. (Written answers, February 8.)

CS

MISS BERNADETTE DEVLIN asked a series of questions about the toxicity of CS and use of the agent in Ulster. She asked whether the Ministry of Defence has ruled out the possibility that prolonged or repeated exposure to CS can lead to accumulation of cyanide in animal tissues, and whether there is any indication that CS can have a deleterious effect on sufferers from asthma. But Mr Ian Gilmour, Under-secretary of State, Ministry of Defence, replied that cyanide is not a cumulative poison and that there is no evidence to suggest that people suffering from asthma are unduly affected by CS. (Written answers, February 10.)

Miscellaneous Intelligence

OPponents of supersonic flight have been slow to point out that the bankruptcy of Rolls-Royce Limited has cast yet another cloud on the Concorde project. Theoretically, at least, the official receiver now in residence at Derby may eventually decide to close down the Bristol Division, the company at present manufacturing Olympus engines, in which case supersonic flight would presumably be delayed for several years. To be sure, a much more likely course of events is that Sud-Aviation would put in an attractive bid for the Bristol Division. Presumably with the interests of shareholders in mind, the receiver in bankruptcy would be compelled to sell, thus helping to ensure that what began as a collaborative aircraft finishes up almost entirely made in France.

THE visit of Mr Andrew Stein, State Representative in the New York State Assembly, seems to have replaced the Federal Aviation Board as the target of those xenophobes in Britain who believe that the United States seeks to hamper British innovation in aircraft by applying footling regulations. Resentment has still not entirely disappeared over the row fifteen years ago when the British aircraft called *Britannia*, named *Whispering Giant* by its advertising agents, was denied a certificate until its landing gear was modified. Mr Stein's apparently innocent bill to limit noise at New York airports to 108 perceived noise decibels

by July and by 98 p.n.d. by 1977 could be such a serious threat to the viability of Concorde that Mr Anthony Wedgwood Benn, once Minister of Technology but still MP for the Bristol constituency in which Concorde is manufactured, is off to New York next week to put the opposing case. But if Mr Stein should get his way, there may still be time to reconsider the best arrangement yet for using supersonic transports—a shuttle service between Newfoundland or Maine and Ireland, with subsonic feeder services from the terminals.

ONE SIGN that may be taken as proof that the polytechnics will in due course be just like other universities is that the students at the North London Polytechnic, an amalgamation of the North-western Polytechnic and the Northern Polytechnic in London, have been protesting against the appointment of Professor T. G. Miller as principal on the grounds that Professor Miller was for two years principal of the University College of Rhodesia. What the polytechnic needs now to establish its claim to be taken seriously as an establishment of higher education is, first of all, a visit from Mr Enoch Powell (whose car can be stopped by shouting crowds) and an opportunity to say no to a speaking engagement by the recent Prime Minister, Mr Harold Wilson, or the present Home Secretary, Mr Reginald Maudling.

Select Committee probes Embarrassing Area

"THE past and present state of Britain's space activities . . . has been a story of wasted opportunities brought about by lack of purpose and the absence of any coherent organization. There has been no real space policy and no space programme as such." Nearly four years ago, the House of Commons Estimates Committee used these words to preface a string of recommendations for reforming the organization of space research in the UK. Few of the committee's recommendations were taken up, most were ignored and there is still no overall policy for British space research.

As a subcommittee of the Select Committee on Science and Technology has discovered from only two public hearings, the vesting of responsibility for much of British space research in the Ministry of Aviation Supply has not helped to coordinate activities. Individual ministries are still responsible for space activities which fall within their own departments' terms of reference, while the Ministry of Aviation Supply sits in the centre, looking after some of the international programme and going its own way with launcher development in the UK. Some indication of the fragmentation of British space research can be gained from the fact that last year out of a total budget of nearly £17 million for national space activities, the Department of Education and Science was responsible for £4 million, the Ministry of Defence for £6.7 million, the Ministry of Posts and Telecommunications for £1.6 million and the Ministry of Aviation Supply for £4.6 million (see *Nature*, 229, 362; 1971). In spite of the fact that the Ministry of Aviation Supply is nominally in the centre of this activity, providing technical assistance and expertise to other departments, when the members of the subcommittee asked questions of representatives from the ministry, they were invariably told that the Ministry of Aviation Supply is not responsible for that particular aspect of research or development. The committee has therefore been unable to glean much information about how priorities are established in planning space research, and there is even a hint of suspicion in the evidence taken so far that such priorities cannot be formulated under the present arrangements.

As far as international cooperation is concerned, Mr Palmer's subcommittee will discover that the British government's attitude has been less than consistent during the past decade. To be sure, this inconsistency is a reflexion of the muddle into which the European organizations have got themselves, but

again there have been difficulties because responsibility for all aspects of international cooperation in space research is vested in several different departments. The Ministry of Aviation Supply is responsible for British participation in ELDO, the Ministry of Posts and Telecommunications for INTELSAT and other post office studies, and the Science Research Council sends delegates to ESRO and negotiates with NASA for the launching of British scientific satellites.

On launcher development, however, a clear policy has emerged during the past few years—the government will not participate in European launcher development if it means duplicating research and development that has already been carried out in the United States. This policy has led to almost complete British withdrawal from ELDO, and is chiefly responsible for the present state of limbo about participation in the post-Apollo programme. While there was an opportunity of using the Blue Streak launcher as the first stage of a small European launcher, the British government enthusiastically supported ELDO, but when the organization decided to go ahead with development of a much larger launcher, Europa 3, the government decided to limit the British contribution to ELDO to £11 million from January 1, 1969. About £10 million of that money has now been spent.

The chief argument behind this policy is that while Europe can buy launchers from the United States, it is wasteful, both in terms of money and resources, to develop an independent European capability. A much better area in which to invest is applications satellites, and the government's policies towards ESRO and in the European Space Conference have been geared towards this end. But this concentration on applications satellites has, in many ways, created more difficulties for organization in Britain—although the SRC is responsible for sending delegates to the ESRO council meetings, the UK contribution to the cost of studies on applications satellites is taken from the Ministry of Aviation Supply's budget. So once again there is split responsibility, and the situation is even more confused by the fact that part of the studies on ESRO applications satellites is concerned with a communications satellite, and this area is usually the responsibility of the Ministry of Posts and Telecommunications.

Although there is plenty for Mr Palmer's subcommittee to get its teeth into when it investigates Britain's international space policies, it is on the domestic front that the subcommittee is

likely to discover the most to criticize. The UK's national space programme falls essentially into three parts, each of which is the responsibility of a separate ministry. The Department of Education and Science has been involved in the development of the highly successful Skylark sounding rocket, 202 launches of which have been made since 1957, and the DES is also responsible for development of a series of scientific satellites in cooperation with the United States. Three of these satellites have now been successfully launched, a fourth is due to be launched later this year, and a fifth in 1973. A defence communications satellite has been developed by the Ministry of Defence, and was launched by the US in 1969. Finally, the Ministry of Aviation Supply is responsible for the development of the Black Arrow Launcher and a series of technological satellites which Black Arrow should place in orbit during the 1970s.

The subcommittee has already asked a few embarrassing questions of the representatives from the Ministry of Aviation Supply about development of the Black Arrow launcher, and it seems that its rather mediocre performance so far is causing some consternation in the committee. Black Arrow is a small rocket, designed to place a payload of 120 kg into a near-Earth orbit. So far, of the three development firings, one has been a success, one failed in the guidance control, and the other failed in the second stage pressurization. Nevertheless, the Ministry of Aviation Supply is going ahead with another launch attempt in the autumn, and the subcommittee was told that a further series of satellites for testing components and subsystems "for use in future satellites" has been suggested for the 1970s. Development of the Black Arrow, it seems, has turned out to be much more expensive than the ministry first envisaged, and the whole programme is due for review later this year.

Mr Palmer's subcommittee will evidently want to satisfy itself that the Black Arrow project is giving value for money, and that the experiments planned for future satellites will provide results that are likely to be useful to other departments. This, of course, implies that British space activities should be much more closely integrated, and that some attempt should be made to coordinate the activities of the various departments. As the Estimates Committee said in 1967, "many departments and many committees have spent much time looking at aspects of space, but it has never been considered as a whole".

NEW WORLD

Earthquakes trigger Reports but no Funds

by our Washington Correspondent

"IMMEDIATELY following a destructive earthquake the public is aroused and, in response, public officials are attentive to the problem. Demands are made for more and better earthquake protection, but memory of the event quickly fades; in a few years, as long as there is no disastrous event, the public feels that everything is under control, and public officials turn their attention to problems seemingly more urgent." Thus a report published in 1969, accurately prophesied the reaction to its recommendations. At least six reports on earthquakes have appeared since the Alaska earthquake of 1964, two apiece from the Office of Science and Technology and the National Academy of Sciences, one from the National Academy of Engineering and one from the Federal Council for Science and Technology.

Each report has arrived at broadly the same list of recommendations. The reports differ only in the amounts of additional research funds that they ask should be made available. As methods of predicting and controlling earthquakes grow less distant, the number of seemingly worthwhile research programmes increases accordingly, so that the requisite investment in earthquake research has escalated from about \$26 million a year recommended by a report in 1965, to more than \$60 million a year by 1969. Government spending has in fact grown from about \$5 million a year in 1965 to \$8 million this year.

It is too early to tell whether the earthquake that shook South California last week will be any more effective than was the Alaska earthquake at opening the doors of treasury vaults. In terms of casualties—probably the crucial factor in securing action—both events have been as sparing of human life as they have been destructive of property. Only 115 people died in the Alaska earthquake—a festival on the pier and waterfront of Seward, wholly wiped out by the earthquake, was cancelled at the last minute—and so far the toll in last week's tragedy is less than 70. But despite the small size of the southern California earthquake, which registered only 6.4 on the Richter scale, damage to property is estimated at about \$1,000 million. It is also disturbing that several of the structures destroyed, including bridges and buildings, were designed to be resistant to earthquakes.

The San Andreas fault, which strikes

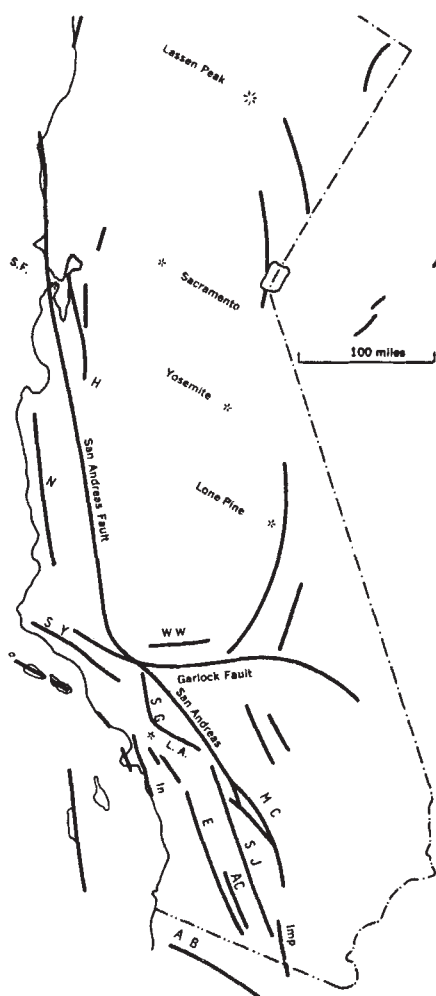
through California on a north-west-south-east axis, has caused two major earthquakes in the past 120 years, one in Los Angeles in 1857 and the San Francisco quake of 1906. Since these events seem to occur once in every 60 to 100 years, another major earthquake—7.75 or higher on the Richter scale—can reasonably be expected at any moment.

Unlike the great majority of earthquakes, which come and go with nobody any the wiser, the southern California earthquake is being fairly well documented. Some 20 portable instruments of the Geological Survey and Coast and

Geodetic Survey have now been moved to the site to record aftershocks, although at the nearby seismic observatory at Pasadena many of the instruments went off their scales during the main shock.

An intensive study of the earthquake is also being planned by the National Science Foundation. Like other agencies with an interest in earthquake studies, however, the foundation's means are insufficient for its needs. A programme of earthquake engineering research, initiated in 1965 in response to the Alaska earthquake, now disposes of \$2 million a year, increased to \$3 million in the budget for 1972, and a total of \$1.5 million is spent on geophysical research related to earthquakes, mostly seismology, laboratory studies of rock behaviour and surveys of the variations in magnetic field across the San Andreas Fault. Other agencies conducting earthquake research include the Geological Survey, which spends about \$1.5 million a year, much of it in support of the National Centre for Earthquake Research in Menlo Park, California, the Atomic Energy Commission and the Coast and Geodetic Survey. There is no coordinated research programme of the type envisaged by a succession of recent reports.

A panel chaired by Professor Frank Press of MIT, for example, prepared a report for the Office of Science and Technology in 1965 entitled *Earthquake Prediction: A Proposal for a Ten-Year Program of Research*. This contained suggestions for studying earthquake generation and prediction, including the installation of a network of seismometers in California and Alaska. The programme should be supported at the level of \$268 million over ten years, of which \$60 million was earmarked for earthquake engineering. The chief result of the report was to initiate two further reports, one of them commissioned by the Federal Council for Science and Technology and the other by the National Academy of Engineering. The council's report, *Proposal for a Ten-Year National Earthquake Hazards Program*, was written by an interagency panel under the chairmanship of Dr William T. Pecora, director of the Geological Survey, and completed in 1968. It recommended a programme essentially identical with that put forward by the Press panel, though with a heavier emphasis on fire hazards and the socio-economic problems associated with earthquakes, and called for a



S.F. San Francisco
L.A. Los Angeles

FAULTS LETTERED AS FOLLOWS:

H	Haywards	AC	Agua Caliente
N	Nacimiento	Imp	Imperial
WW	White Wolf	AB	Agua Blanca
In	Inglewood	SY	Santa Ynez
E	Elsinore	MC	Mission Creek
SJ	San Jacinto	SG	San Gabriel

ten year budget of \$218 million, exclusive of engineering research.

The National Academy of Engineering, for its part, produced in 1969 a report devoted to the engineering aspects of earthquakes, *Earthquake Engineering Research*, which proposed the expenditure of \$38 million a year over a ten year period for those aspects alone. The report, produced by a committee chaired by Dr George W. Housner, of CalTech, urged the setting up of a panel to coordinate research carried out by the various government agencies and universities, and suggested that the National Science Foundation should assume the lead in directing the research effort.

1969 was a good year for reports about earthquakes and two more were to erupt before the year was out. *Toward Reduction of Losses from Earthquakes*, issued by the committee on the Alaska earthquake of the National Academy of Sciences, presented in summary form the main recommendations deduced from study of the 1964 earthquake. These included the call for more research into the development of earthquake resistant structures, earthquake forecasting and loss reduction, as well as for improved arrangements for gathering seismic data. A second report, produced by the committee on seismology of the National Academy of Sciences, repeated the plea for a national ten-year effort in seismology, the major part of which, it says, should be devoted to research on earthquake hazards and earthquake prediction and control (*Seismology: Responsibilities and Requirements of a Growing Science*). The committee envisaged that federal support of seismology, then running at about \$10 million a year, should increase to \$35 million by fiscal year 1971, and then to £50 million and above, making a round total of \$500 million over the decade of the 1970s. Earthquake-related items in this imagined budget included \$175 million to be devoted to prediction and prevention of earthquakes (exclusive of engineering), \$55 million for instrumentation and observation and some \$40 million for studying the physics of earthquake processes, making a total of some \$270 million.

The chief difference between NAS and NAE reports of 1969 and the OST report of 1965 was that the latter proposed a ten year budget of \$218 million for geophysical and other research, and \$60 million for engineering research, while the former reports proposed sums of \$270 million and \$380 million respectively for these two categories of research. Perhaps because all these reports had only a token effect on federal expenditures, the most recent government effort in this direction avoids all mention of money and merely repeats the same list of recommendations.

Earthquake Hazard Reduction, issued

last September by the Office of Science and Technology, is the report of a task force chaired by Karl V. Steinbrugge. The report counts earthquake prediction and control as benefits likely to accrue after a ten year research programme: projects likely to reap immediate reward include requiring all federal buildings to be of earthquake resistant design and preparing better seismicity maps. Applied research on earthquake engineering is deemed likely to yield fruits 5 to 10 years after commencement. The OST invited federal agencies to submit their comments on the Steinbrugge report, which were due in last month, but has taken no further action.

All six government reports prepared in the last six years have had less tangible effect than the utterances of the young clairvoyante, who predicted in 1968 that a catastrophic earthquake the following April would cause California to slip into the ocean; she at least produced a sharp increase in the airline reservations

for flights out of California in March. It remains to be seen whether last week's earthquake will give any greater credence to the warnings of seismologists. But one thing seems certain: another report will be called for.

SEISMOLOGY

California Quakes Again

by our Geophysics Correspondent

THE most recent seismicity maps of the Earth show the San Andreas fault and its parallel neighbours as remarkably patchy features. For the most famous and most studied fault system in the world does not reveal itself by a regular chain of earthquakes along its thousand kilometre length, but by some regions of high seismicity interspersed with others of little or no activity. Future prospects in these quiet zones are obviously a very important matter and the evidence so far

Latest Lunar Seismology

LATEST reports are that the Apollo 14 seismometers are performing well and revealing very similar phenomena to those recorded by the Apollo 12 seismic package. The latter is still operating satisfactorily over a year after its installation (and beyond its nominal lifetime) and recorded the impact of the Saturn IVB rocket on the Moon. Again the extraordinary seismic records were seen with discernible compressional and shear waves and then the build-up and long ringing decay in energy over a space of two or three hours. The LEM impact was aimed between the two instruments and fills in two further points on a lunar travel time curve which is now quite well populated with impacts from LEMs and rockets. Starting from laboratory determinations of compressional velocity as a function of pressure for collected Moon rocks, it is possible to predict a velocity-depth function for the Moon which tallies remarkably well with the inferences from travel-time data now available.

The first part of the active seismic experiment—obtaining surface seismic velocities by thumping the ground in the vicinity of the Apollo 14 seismometers also appears to have worked well and yielded very low velocities (less than 100 metres/sec) for P-waves in the first few metres. The more spectacular experiment—the firing of mortars which land at distances between the thumper range and those of the impacts—has yet to be started.

The source of the ringing is still uncertain. Recent geophysical meetings have spawned an inordinate number of (often ill-informed) explanations. The front-runner at the present, however, seems to be this. The Moon rocks are assumed to have a combination of two properties not observed together on Earth—a high Q, or low absorption of seismic energy, and a heterogeneity sufficient to scatter seismic waves strongly. The incoherent but long lasting signal is the result—akin to the long rumble of thunder scattered by inhomogeneities in the atmosphere.

Meanwhile natural seismic activity continues to be recorded by the Apollo 12 instruments, and it is hoped that the addition of the second set of triaxial instruments will help to pin down the source of this activity. There are some intriguing facets. The peak of the activity seems definitely correlated with the lunar month—a correlation never satisfactorily pinned to any Earthly seismicity. In addition the events are carbon copies of each other—the traces tally wiggle for wiggle over extended periods. This in conjunction with the incoherence between different components of the ground motion is a very strong restraint on the location of the events. Experience in similar situations on Earth with heterogeneous media and scattering has shown how extremely sensitive the seismic signal is to the location of the source. Moving the source a few metres may change the whole pattern. Are the Moon events that close to one another? At the moment, it looks like it, in which case some form of venting would be the most obvious candidate.

is hopeful in some cases, gloomy in others. It seems that parts of the fault system are undergoing a continual relieving slippage not associated with earthquakes. The rest of the quiet zones must be just accumulating strain. It is generally agreed that the Pacific Plate and the North American Plate, whose boundary is the San Andreas system, are moving in a right-handed sense at 5 cm a year relative to each other. The best evidence is that fault movements during earthquakes are unlikely to exceed a few metres, so catastrophic quakes may be expected to occur every few tens of years in quiet zones where there is no slipping.

Viewed in this simple light, the earthquake north of Los Angeles appears to fit neatly into the framework. There has been no major earthquake near Los Angeles since 1857 when there was a shock comparable with the 1906 quake in San Francisco with a rupture length of at least 200 km. There have been relatively few minor earthquakes in this region in comparison with most other parts of the San Andreas fault. So if the fault was not slipping, all the signs were that something would have to go eventually. And yet the quake does not fit into this scheme of things and there is doubt among seismologists in the region whether it has done anything at all to relieve the accumulated strain.

The problem is this. The best estimate so far of the location of the event is that it is 15 km north of San Fernando and 50 km north of downtown Los Angeles. Talking about a location is perhaps unrealistic for an earthquake of a magnitude of 6.5 for which the horizontal dimension of the faulting region is likely to be at least 10 km, probably much more. This whole region is completely intercepted with faults, none of which is dominant, but it can be stated with considerable confidence that the fault which moved was not the San Andreas. Nor indeed does it seem from first reports to have been the San Gabriel—a fault which runs parallel to the San Andreas. Instead it has been suggested that the ground displacements are on the Soledad Canyon Fault—a fault which appears on practically none of the maps of the area and has no known seismic history. Further, the motion does not seem to have been the right-handed strike slip associated with the San Andreas.

Much more will be known shortly when the intensive field work starts to be reported on and it will be foolish to speculate on the basis of incomplete information, but the following general points can be made. The event occurred in a region which had been relatively free of activity and seems to have a mechanism that is not immediately seen to be that of the San Andreas. This emphasizes in a dramatic way the unpredictability of seismic activity. The

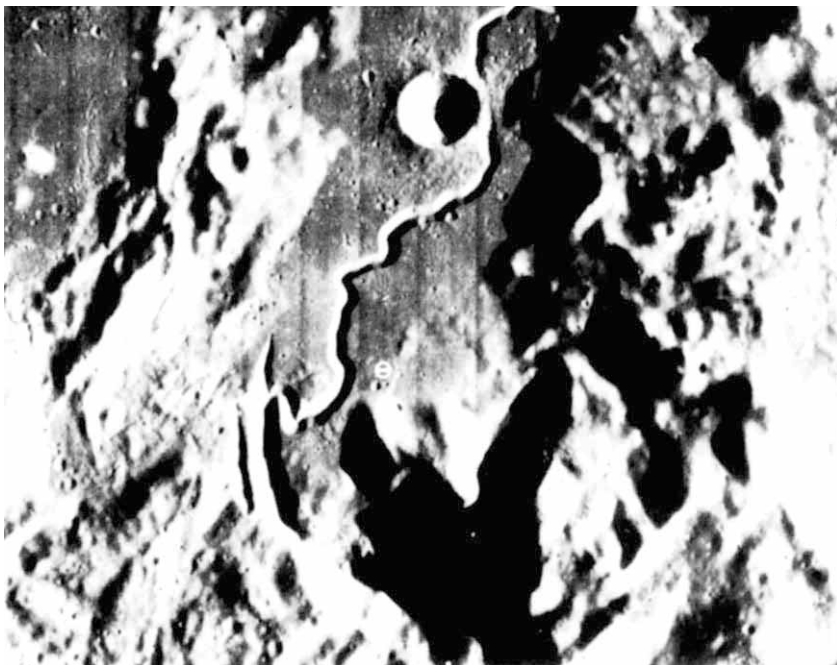
remarkable successes of plate tectonics are based on observations of the narrowness of most seismic belts and the consistency of earthquake mechanisms, with the idea of these belts being boundaries between moving plates. However, it is worth repeating that plate tectonics appears to be only a guide line in continental regions. Relatively new ocean crust is not intersected with pre-existing faults—continental crusts having been the object of violent forces for the past 4 billion years have much inactive faulting completely unrelated to present activity. Small wonder then that the stresses of present day movement lead to major activity away from the plate boundary as old faults take up the strain and accommodate to the latest forces. A compilation by C. R. Allen *et al.*, in the *Bulletin of the Seismological Society of America* in 1965, shows the contours of strain relief in a 30 year period to have distinctly contradictory relations to the San Andreas, and major fault movements have occurred at all angles to the San Andreas trend and at distances of up to 200 km from the main fault.

This leads to the second point—that earthquake prediction and control in a region like California require more than monitoring the major faults and (maybe) attempting to relieve strain on

them. If a relatively unknown fault can suddenly break, then any reasonable effort at monitoring must be on a very broad and comprehensive basis. Fortunately there is growing interest in the work, but it is a long term project with an unclear prospect of success even in 50 years. Funding in science tends to be so oriented towards immediacy that seismologists should perhaps look to new sources—maybe more extensive support from those businesses which suffer the severest financial losses by earthquakes—insurance companies.

Thirdly, it bears repetition that there is no evidence whatsoever to associate earthquakes with unusual lunar coincidences such as the eclipse which occurred 12 hours later. Already some zealous quacks seem to have forgotten that the earthquake came before the eclipse and are claiming the effects of the eclipse were seen immediately afterwards in the quake. The Moon and Sun do indeed raise tides on the solid Earth of 30 cm but no one has yet pinned down any seismic phenomena to high tide on the Earth—and many have tried. Of course, the plane of the Moon's orbit is close to that of the ecliptic, so talk of the eclipse being an unusual strain to the Earth is idle nonsense when eclipse type conditions prevail to first order twice every lunar month.

Target for Apollo 15



With the Apollo 14 astronauts safely home, the portents are better for the next in the series, scheduled for July this year. The aim is to obtain samples from the vicinity of the Hadley Rille, and one of the landing sites which has been under consideration is marked. This time the astronauts will have the use of a roving vehicle to visit the foothills of the nearby Appenine mountains, but they will not be going into the rille itself, which is 600 feet deep. On the Orbiter photograph of the area the large crater adjacent to the rille is Hadley C, about 5.5 km across. The location of the area is at 26° 52' N, 3° 00' E.

NEWS AND VIEWS

Isolation of the Cholinergic Receptor Protein

It has been clear for some time that progress in the application of the techniques of molecular biology to understanding the pharmacological problems of drug receptor interaction required the ability to isolate and purify the receptor macromolecules involved. The paper by Miledi, Molinoff and Potter on page 554 of this issue of *Nature* which describes the isolation of a cholinergic receptor protein thus represents an important landmark in the development of molecular pharmacology.

The isolation of receptor macromolecules, as in any other protein purification, depends first on the availability of an abundant source material. Fortunately, nature has provided such a source in the form of the electric organ tissues of electric fishes and eels, in which there is an extremely dense cholinergic innervation of the electrical tissue and an abundance of postsynaptic cholinergic receptors which are indistinguishable in their pharmacological properties from those which exist at much lower densities at vertebrate nerve-muscle junctions. A more difficult problem has been the development of methods by which the receptor macromolecule might be identified in solubilized preparations of the membrane protein of excitable membranes. In the intact tissue the receptor can be defined operationally as 'that entity with which acetylcholine interacts to cause a change in the ionic permeability of the innervated cell membranes; such a criterion clearly cannot be applied once the receptor has been removed from the membrane. Many attempts have therefore been made to identify the cholinergic receptor by using acetylcholine or various analogues of acetylcholine on the assumption that the cholinergic receptor must possess a high affinity binding site for such molecules. Although in principle such an approach is acceptable, in practice there has been rather little success so far in the application of "cholinergic ligands" for identifying receptor macromolecules, because of the existence of many cholinergic binding sites other than the cholinergic receptor in excitable membranes, including the catalytic and allosteric sites of acetylcholinesterase. For similar reasons, there has also been only limited success in the use of reversible cholinergic antagonists, such as D-tubocurarine or atropine, as receptor labels.

This methodological impasse, however, now seems to have been overcome, and, as so often in the past, the solution lies in the application of a natural product of exotic origin and extraordinary specificity. The *deus ex machina* in this case is a snake venom toxin, α -bungarotoxin. This substance is a basic polypeptide of molecular weight 8,000 isolated from the venom of a snake from Taiwan (*Bungarus multicinctus*). α -Bungarotoxin was isolated and studied by Lee and his colleagues at the National University of Taiwan, who showed that the toxin acted as an irreversible antagonist of cholinergic receptors at vertebrate nerve-muscle junctions. They also demonstrated that this effect could be prevented by D-tubocurarine, which is a specific but reversible antagonist of neuromuscular cholinergic receptors, indicating that α -bungarotoxin interacted with the cholinergic receptors.

The recent report by Changeux, Kasai and Lee (*Proc. US Nat. Acad. Sci.*, 67, 1241; 1970) and the current paper by Miledi *et al.* in this issue describe the use of α -bungarotoxin to characterize the cholinergic receptor protein of electric organs. Changeux *et al.* found that α -bungarotoxin blocked the responses of cells in the intact electroplaques of *Electrophorus electricus* to the acetylcholine analogue carbamylcholine, and that this effect was irreversible. They also showed the same effects of bungarotoxin in an *in vitro* system, in which carbamylcholine normally increased the sodium permeability of isolated membrane fragments prepared from the electroplaques. In this preparation D-tubocurarine protected against the irreversible blocking effect of bungarotoxin, and the actions of bungarotoxin seemed to be irreversible and stoichiometric; the amount of toxin needed for complete receptor blockade was directly related to the amount of membrane material present. The actions of the toxin also seemed highly specific, because additions of membrane material prepared from the non-innervated face of the electroplaques in which cholinergic receptors are absent did not significantly decrease the antagonist effect of the toxin on innervated membrane fragments. It would seem therefore that the cholinergic receptors of the electroplaques could be titrated in a highly specific manner with bungarotoxin. The specificity of action of the toxin was also confirmed by the absence of any effect on the activity of acetylcholinesterase. Changeux *et al.* were also able to estimate the number of cholinergic receptor sites in the electroplaque tissue from the minimum amount of bungarotoxin needed to produce complete receptor blockade, and concluded that the number of receptor sites was approximately equal to the number of acetylcholinesterase catalytic sites in the tissue. Finally, Changeux *et al.* reported that bungarotoxin irreversibly inhibited the binding of radioactively labelled decamethonium in a soluble preparation of electroplaque membrane protein, suggesting that bungarotoxin could be used to identify the cholinergic receptor macromolecule in such soluble preparations.

Miledi, Molinoff and Potter have exploited the extraordinary specificity of bungarotoxin to the extent of isolating and purifying by this means what seems to be the cholinergic receptor protein. Miledi *et al.* first confirmed that α -bungarotoxin acted as an irreversible antagonist at cholinergic receptors in the electric tissue of *Torpedo marmorata*, and also at neuromuscular junctions in frog sartorius muscles. Miledi *et al.* also prepared radioactively labelled bungarotoxin of very high specific activity by iodination with ^{131}I . This material was used to study the binding of toxin to cholinergic receptor sites in a preparation of membrane fragments from disrupted electric tissue. The binding of labelled toxin was dependent on the time of incubation and the concentration of toxin, and was saturable. The rate of binding of labelled toxin was decreased in the presence of D-tubocurarine or carbamylcholine, but was unaffected by the acetylcholinesterase inhibitor physostigmine or by sodium dodecylsulphate, suggesting a specific binding of the toxins to

cholinergic receptors. It proved possible to release the labelled toxin-receptor complex from the membrane fragments by treatment with a low concentration of the detergent 'Triton X-100', and the toxin-receptor complex was then purified by chromatography and density gradient centrifugation. On chromatography in the presence of detergents the toxin-receptor complex could be clearly separated from the enzyme acetylcholinesterase. The purest fractions obtained contained 1 μg of bungarotoxin per 10 μg membrane protein, suggesting a molecular weight for the receptor protein of approximately 80,000. In the absence of detergent, the receptor protein formed aggregates of 500,000–2,000,000 molecular weight. In low concentrations of 'Triton' the receptor protein seemed to consist of a tetrameric form of the 80,000 molecular weight subunits. As in the experiments of Changeux *et al.*, the number of bungarotoxin binding

sites in *Torpedo* tissue was approximately equal to the number of acetylcholinesterase catalytic sites. If the receptor protein normally exists as a tetramer, as is the case with acetylcholinesterase, this would imply that the electric tissue membrane contains equal numbers of enzymes and receptor molecules. Miledi *et al.* estimated the number of bungarotoxin binding sites as approximately 10,000/ μ^2 of cell membranes.

Although the present reports from the Paris-Taiwan and London groups are clearly preliminary, it would seem that the use of bungarotoxin is well grounded on pharmacological evidence. These findings thus offer a great potential for future studies on the molecular mechanisms involved in drug-receptor interaction. Pharmacologists and molecular biologists may be justified in wondering whether this does not constitute at least a partial redemption for the serpent.

Aftermath of the Revolution

THE importance of the article by Baker and Wohlenberg on page 538 of this issue of *Nature* lies as much in the philosophy behind it as in the geological and geophysical knowledge it embodies. For it acknowledges that geology is coming to terms at last with the global model of the Earth which geophysics has imposed on it; and it marks the end of the fear that the vast intellectual edifice constructed by geologists since the ages of Hutton and Lyell must be completely demolished in the light of the new global tectonics. The reality is, of course, far less severe than the fear. For a century or more geologists were much concerned with detailed examination of small regions of the Earth's surface, from which they would attempt to generalize to the larger world. The problem was that, through no fault of their own, they were never able to generalize successfully to the extent of constructing a valid world model. That geophysicists have in less than ten years been able to do just that proves not so much that the geologists were wrong but only that the tools at their disposal were not up to the task.

The way ahead is thus not to destroy the old geology but to reinterpret its legacy in terms of the new global tectonics. And to their credit, Baker and Wohlenberg have recognized this. The purpose of their article is, they say, "to summarize modern geological knowledge of the Kenya rift and to reconcile this with crustal models and kinematic concepts derived primarily from geophysical data". They are surely right in seeing this as the logical procedure to follow in the wake of what J. Tuzo Wilson has so aptly termed the revolution in the Earth sciences.

The scientific point to emerge from the reconciliation is not perhaps the surprise it would have been a few years ago. Baker and Wohlenberg conclude that although the East African rift is linked to, and at first sight seems to be a continuation of, the world oceanic ridge system, it is neither typical of that system nor probably an example of the first stage of continental breakup. In rejecting the idea that rift valleys are the simple land based equivalents of the median valleys of oceanic ridges, and in attributing the former instead to "long-continued interaction between crust and thermally activated mantle", Baker

and Wohlenberg have thus followed a different route to arrive at a conclusion similar to Murray's (*Earth Planet. Sci. Lett.*, 9, 34; 1970), which was based on geochemical evidence. At the same time they confirm the suspicions generated by the discovery that the heat flow over the East African rift is, if anything, lower than the world average and not abnormally high as over oceanic ridges.

There is, of course, some irony in that although Baker and Wohlenberg have enthusiastically embraced the new global tectonics, they have been instrumental in destroying one of its most cherished myths. But there is no harm in that. If geophysicists have a fault it is that they have sometimes tended to exaggerate the extent to which the simple tenets of global tectonics apply to the real world. So there is nothing to be lost by a few counterbalancing jolts from time to time. It is a pity, though, that when Baker and Wohlenberg wrote their article they did not have at their disposal the seismic refraction and gravity data from the Gregory rift described a few weeks ago by Griffiths *et al.* and Khan and Mansfield in *Nature Physical Science* (229, 69 and 72; 1971). The crustal model proposed by Khan and Mansfield, in particular, is somewhat different from those proposed earlier; and to this extent Baker and Wohlenberg may have wished to revise some of their details in the light of the new evidence.

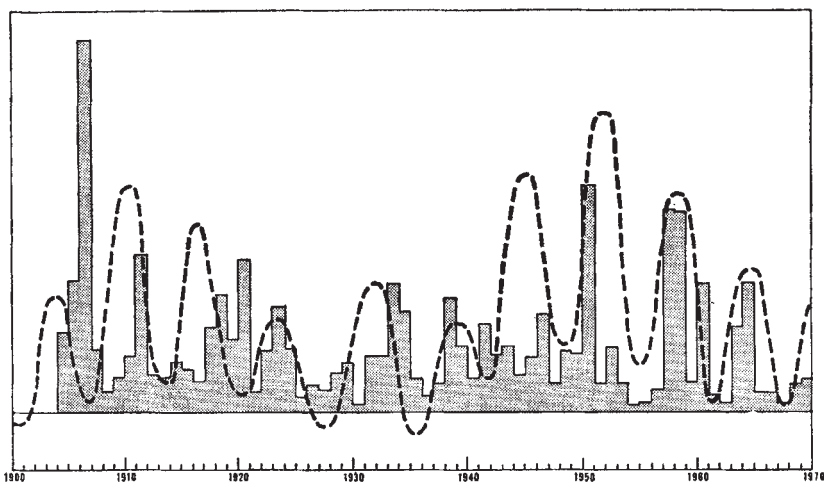
Surprisingly, perhaps, the seismic refraction study of the Gregory rift carried out recently by Griffiths *et al.* was the first attempt to determine the detailed crustal structure in this region. In spite of the widespread interest in the East African rift, first as an extension of the world-wide system and now because it is thought to be in some respects different from the rest of the system, the amount of work done there is remarkably small. Which is a pity. For one reason or another the large American geophysical community has never taken much interest in this important region; and what studies there are have been carried out chiefly by British and Kenyan scientists working either separately or in collaboration.

In view of the importance of finding out just what are the differences and similarities between the East African rift and the oceanic ridges, the time has surely come to mount a geophysical and geological attack on this region.

EARTHQUAKES

More Correlations

from our Geomagnetism Correspondent



The correlation of mean daily polar shift (dotted line) with annual energy released by earthquakes (hatched area).

CORRELATIONS between very large earthquakes and sudden changes in the centre of Chandler wobble by Mansinha and Smylie (*J. Geophys. Res.*, **72**, 4731; 1967) certainly seem to have generated a renewed interest in what, superficially, may seem a dull and not very important problem. As a result of their discovery Mansinha and Smylie suggested that the Chandler wobble may, in fact, be maintained by earthquake energy, though Ben-Menahem and Israel (*Geophys. J.*, **19**, 367; 1970) soon showed that this could not be so. Then Myerson entered the field (*J. Geophys. Res.*, **75**, 6612; 1970) with correlations between the yearly count of earthquakes with magnitudes greater than 7.0 and the rate of change in the Chandler amplitude squared; and concluded from this that although the Chandler wobble may not be a direct result of earthquakes, both phenomena could well be consequences of a third.

This upsurge of interest in an old problem now seems to have affected Whitten (*Earthquake Research in ESSA 1969-70*, p. 7, US Government Printing Office, 1970). Just how Whitten acquired his enthusiasm for this topic is in itself an interesting phenomenon and throws a fascinating light on how scientists come to the problems they try to solve. In 1969, it seems, Whitten attended a conference at which Mansinha and Smylie's work took pride of place and was moved to study the problem himself—with some interesting consequences. The Chandler wobble has a period of about 14 months; but there is also an annual wobble term which has a different origin. Whitten noticed that in order to get at the Chandler wobble proper Mansinha and Smylie had subtracted out the annual term. There is, of course, nothing wrong with that. Mansinha and Smylie were only interested in the cause of the Chandler wobble and thus tried to

eliminate the non-Chandler contribution to the polar shift. As Whitten points out, however, the Chandler and annual wobbles cannot be separated all that neatly; and so he decided, instead, to compare the energy released by earth-

quakes with the total daily polar shift.

When the 12-month and 14-month wobbles are out of phase with each other the daily polar shift is very small because the amplitudes of the two wobbles are similar. But when the two wobbles are in phase the daily motion can be as high as 15 cm. The combination of the Chandler and annual wobbles thus causes a variation of daily polar shift with a periodicity of about 7 years. What Whitten has discovered is that there seem to be more large earthquakes when polar motion is at a maximum (see diagram). To be sure, the correlation is not perfect—particular anomalies are the San Francisco earthquake of 1906 and the Chile earthquake of 1960.

What this says about the cause of Chandler wobble or of earthquakes is not clear. Whitten is inclined to believe that the daily angular shift of the axis of rotation could create additional strains in seismic regions and thus acts as a triggering mechanism. Be that as it may, the consequences of Whitten's correlation in terms of earthquake prediction are even more significant, for we are now at about maximum polar shift. With three large quakes within the past month, Whitten's diagram becomes very interesting indeed.

Free-Radical Substitution at Metal Atoms

BIMOLECULAR homolytic substitution reactions of the type $A \cdot + B-C \rightarrow A-B + C \cdot$ are common in organic chemistry. A, B and C represent atoms or groups. B (the group transferred) is usually hydrogen or a halogen atom; it can (less commonly) be an oxygen or sulphur group. Direct substitutions at saturated carbon rarely occur.

In next Monday's *Nature Physical Science*, Davies and Roberts of University College, London, argue that S_H2 reactions of this type are very common at metal centres in organometallic compounds, and that most involve the displacement of an alkyl radical $R \cdot$ from a non-transition metal compound MR_n by a radical $X \cdot$.



Examples of radicals which can effect S_H2 reactions include alkylperoxy, alkoxy, sulphur, dialkylamino, succinimido, and alkyl radicals, as well as halogen atoms. A wide range of organometallic metal atoms can be attacked and boron and tin compounds feature prominently. Direct evidence for reactions such as (1) is provided by ESR studies; for example t-butoxy radicals will displace alkyl radicals from boron trialkyls. The alkyl radicals can be detected by ESR, and this seems to be a useful method for production of specific organic radicals.

There is a great deal of evidence that

autoxidation of boron trialkyls and other organometallics occurs by a radical chain reaction (reactions 2 and 3), in which reaction 2 is an S_H2 reaction on the metal atom.



Autoxidation of hexa-ethylditin is thought to proceed analogously; an $Et_3SnOO \cdot$ radical is assumed to displace an $SnEt_3 \cdot$ radical from $Et_3Sn-SnEt_3$.

The reaction of N-halo-succinimides with tetra-alkyltins is interesting. A chain mechanism is postulated ($Suc \cdot$ is the succinimide radical).



A number of reactions of halogen atoms are interpreted in terms of S_H2 attack at metal centres, for example the reactions with organomercurials; heterolytic mechanisms often compete in these reactions. Alkyl radicals seem to attack metal centres by S_H2 reactions (for example, boron, silicon, tin and mercury).

Davies and Roberts conclude that recognition of S_H2 mechanisms frequently offers the key to understanding familiar organometallic reactions and to the prediction of new ones. Physico-chemical studies are needed to discover the way in which electronic and steric effects control the rates of these reactions.

ARCTIC GEOLOGY

Basin Drift

from our Structural Geology Correspondent

THE declared theme of the symposium on Arctic geology, organized by the American Association of Petroleum Geologists and held in San Francisco during February 1-4, was the regional geology of the Arctic. This subject was convincingly and comprehensively covered by some thirty contributors, but most interest was perhaps aroused by the discussions of petroleum exploration and the evolution of the Arctic Ocean Basin.

At the time of the 1960 symposium ideas of seafloor spreading and the associated concept of plate tectonics were in their infancy. Consequently many of the earlier hypotheses for the evolution of the Arctic Ocean Basin have had to be substantially modified. As pointed out by Dr N. A. Ostensio (Office of Naval Research, Arlington), the unique situation of the Arctic Ocean, bordered by both the New and Old Worlds and linking the Atlantic Ocean with the Pacific Ocean, presents a key to understanding not only the present spreading movements but possibly also the older plate arrangements.

The Arctic Ocean consists of two distinct oceanic basins—the Eurasia Basin and the Canada Basin, separated by a strip of continental crust, the Lomonosov Ridge. The Eurasia Basin was shown by means of symmetrical magnetic anomaly striping to have opened during the past 30 million years; its central spreading ridge was connected by means of the De Geer transform fault to the mid-Atlantic spreading ridge. The Lomonosov Ridge would thus represent a piece of the Barents Shelf carried westwards by spreading. The Canada Basin seems to be an older oceanic basin with no pronounced magnetic striping. Views concerning its origin were varied, but most speakers, including Dr I. L. Tailleux (US Geological Survey), favoured its opening during Late Mesozoic by means of a pivotal action about the Alaskan Orocline which would have involved the rotation of Alaska away from the Arctic Canadian Islands, a situation well substantiated by surface geology.

Baffin Bay and its connexion by way of the Davis Straits to the Labrador Sea and the Atlantic was shown (J. W. Kerr (Geological Survey of Canada), and others) to have opened by the drift of Greenland away from Baffin Island pivoted on Ellesmere Island in the Canadian Arctic. Thus the present Arctic Basin seems to have developed during the most recent stages of seafloor spreading, in contrast with the Pacific which it would seem presents a constant physiogeographic feature at least since the beginning of Phanerozoic time.

Measuring the Invisible

FIFTY years ago a distinguished Rolls-Royce engineer, A. A. Griffith, postulated an explanation for the fact that the tensile fracture strength of brittle solids such as glass is surprisingly low and moreover statistically very variable. He proposed that the surface is pitted by many submicroscopic cracks which can locally amplify an applied stress.

Circumstantial evidence has long since established Griffith's hypothesis beyond all cavil. Practical improvements in the strength of glass and other brittle materials have been based on Griffith's recognition that the surface determines strength; strength can be increased by either removing the cracks through etching or otherwise, and at once protecting the surface by means of a hard coating, or by prestressing a thin surface layer in compression.

Throughout all such technological developments, Griffith's microcracks have remained shadowy entities, apprehended but not seen. A number of methods have been tried to make them visible: plenty of cracks were revealed, but there are reasons for believing that the treatment may create more new cracks than it enlarges old ones.

Next Monday's issue of *Nature Physical Science* includes an article by J. D. Polonietcki and T. R. Wilshaw which establishes a new way of tackling the problem. The technique is the Hertzian fracture test. A hard sphere (here a tungsten carbide ball 0.77 mm in

diameter) is pressed into the glass surface under continuous observation until a ring crack suddenly spreads and grows concentrically with the indentation. The radius of this crack, r_c , and the load P at which it forms are recorded, and the test is repeated many times. The ring radius and critical load are related to the surface density of microcracks of various depths, and therefore in principle it is possible, from distributions of r_c and P , to deduce histograms of surface densities of cracks as a function of crack-depth. This has been recognized for some years, but the problem has been to find an acceptable way of analysing the data statistically. Most previous investigators have been content to postulate a particular form for the histogram (a "Weibull distribution"), which prejudices the central issue. Moreover, nobody has proposed simultaneous analysis of the distributions of both r_c and P .

Polonietcki and Wilshaw's investigation is the outcome of a collaboration between a fracture mechanics expert and a statistician, and it now seems that the analytical problem has been solved. The critical step is to assess the surface area "at risk" in each individual test, and to sum these for all the tests: this total area at risk is different according to the particular range of crack depth under assessment, and has to be separately estimated for each bar of the histogram. The technique has been applied to mechanically polished silica glass and a log/log histogram produced, complete with 90 per cent confidence limits.

Source Counts and Astronomical Evolution

THE game of counting astronomical sources as a function of brightness to test whether they are distributed uniformly throughout space seems to have been invented by Newton.

In the 1960s, the radio astronomers, after a false start based on the ill-starred second (2C) Cambridge catalogue, agreed that they had shot down the steady state theory with radio source counts. The 4C and 5C surveys showed, however, that the unexpectedly steep increase in the number of sources with decreasing brightness did not continue indefinitely, and in fact were at first interpreted as implying that we had seen right back to the epoch at which the galaxies giving rise to the radio emission were formed. This would have been a spectacular result, but unfortunately turned out not to be the only possible interpretation of the source counts.

When the results of the deep Cambridge surveys were confirmed by counts performed by the radio astronomy group at Bologna, it looked as if the observational situation, at least, was sewn up. A cloud appeared on the horizon recently in the form of counts of 8,100 sources surveyed by the group at Ohio

State University (Harris, Beverly and Kraus, *Nature*, 227, 785; 1970). The OHS surveys were done at a slightly different frequency to those at Cambridge and Bologna (1,415 MHz instead of 408), but on conversion they gave significantly fewer faint sources than the latter, though agreeing in the number of bright sources.

In next Monday's *Nature Physical Science* Jauncey and Neill of Cornell University describe some observations which seem to clear up the discordance. Using the NRAO 300 foot dish, which at 1,400 MHz has considerably better resolution and sensitivity than the OHS instrument, they have checked the OHS flux density scale. They found that the random errors are greater than those quoted (which would tend to increase the number of faint sources found) and, more importantly, that the flux densities of the weaker sources are systematically underestimated. This latter bias was confirmed by comparing the OHS catalogue with others done at the same frequency at Cal Tec and at Parkes. Correcting for the bias brought the source counts into agreement with the Cambridge and Bologna counts.

PULSAR MODELS

Agreement at RAS

by our Cosmology Correspondent

IN only three years pulsars have been reduced from the centre of attention among astronomers to the mundane level of routine work. This rapid decline was clearly evident at the specialist meeting on pulsars held by the Royal Astronomical Society on February 12, which contrasted sharply with the first RAS meeting after the announcement of the discovery of these unusual radio sources, or, more recently, with the similar specialist meeting on X-ray astronomy held in November last year (see *Nature*, **228**, 715; 1970). At these earlier meetings, there was a great deal of variety in the ideas and observations presented, with many questions and other contributions from the floor. But at the more recent gathering, only different versions of the same basic model were presented, and very few new observations. The magic word "pulsar" still had sufficient charisma to attract a large audience, but this remained on the whole passive, so that the individual speakers and the whole meeting ran almost exactly to the planned schedule—a very unusual occurrence, and one which is not necessarily a good sign.

Before discussion of the theory of pulsar mechanisms, Professor F. Graham Smith (Jodrell Bank) presented the by now familiar data obtained from the addition of many successive pulses from a pulsar, which seem to show a variation of pulse arrival time over a "window" which remains constant and very well defined. Together with the polarization evidence, this suggests strongly that the regions producing pulsar radiation are confined to a local area (covering some 10° in longitude) on the underlying neutron star; the size of this allowed area defines the observed window, and the small degree of variation in longitude within this region can explain the secular variation frequently observed over several successive pulses. Presumably, this variation is related to the degree of flexibility in the magnetic field which is now almost universally accepted as the beaming mechanism.

The first person to present the pulsar model was Professor L. Mestel (University of Manchester), who made the most of his opportunity to address a still receptive audience, outlining the oblique rotator model which stands unchallenged because of its ready explanation of the timing mechanism of pulsars. This model is based on the natural assumption that a rotating neutron star may have an associated magnetic field, and that the magnetic polar axis is unlikely to be the same as the star's spin axis. It is equally implausible that the magnetic axis would be at right angles to the spin axis, but

consideration of these two extreme cases shows how the more probable intermediate cases may produce interactions leading to beamed radiation.

Streaming of charged particles outwards along the magnetic lines of force in this kind of model naturally leads to a situation where they are moving in a circle close to the speed of light, because although the magnetic field may lag behind the solid rotation of the underlying neutron star it must rotate almost as a solid body. Rotation at constant angular velocity then implies that sufficiently far from the star the field is rotating at the speed of light. The silent majority seemed happy to accept this idea as a now well established fact, especially when it was presented three times in rapid succession, with only relatively

minor problems remaining to be solved. In one interpretation, the outward flow of plasma only reaches relativistic velocities (and produces beamed synchrotron radiation) where the magnetic field is travelling at twice the speed of light, and there was some discussion of the detail of the kind of magnetosphere which would agree with the observed radiation. To an outside observer the fire and excitement has definitely gone out of the pulsar hunt. Indeed, the experts are so blasé that they accepted the news that the Crab pulsar's so-called precursor pulse is completely absent at a frequency of 606 MHz (see *Nature Physical Science*, **229**, 192; 1971) without comment, even though this pulse is the strongest of the three seen in NP 0532 at half this frequency.

Identification of X and Y-bearing Human Sperm

It has been shown recently that some fluorescent dyes such as quinacrine mustard stain certain chromosome regions in a specific fashion. Of particular interest is the discovery that the distal end of the long arm of the human Y chromosome has a very characteristic fluorescent band (L. Zech, *Exp. Cell. Res.*, **58**, 141; 1969) enabling its detection in mitotic and meiotic cells as well as in interphase nuclei. Last year, two groups of workers (P. L. Pearson and M. Bobrow, *J. Reprod. Fert.*, **22**, 177; 1970; and P. Barlow and C. G. Vosa, *Nature*, **226**, 961; 1970) reported that slightly less than 50 per cent of mature human sperm stained with quinacrine contain a fluorescent spot and these were tentatively identified as Y-bearing sperm.

In next Wednesday's *Nature New Biology*, Sumner, Robinson and Evans report their findings from a study of sperm from nine chromosomally normal individuals. Their results confirm that just under 50 per cent of mature sperm contain a fluorescent spot. In view of the fact that the human X chromosome is much larger than the Y, they point out that Y-bearing sperm should contain significantly less DNA than X-bearing ones. Using fluorescent staining followed by optical density DNA measurements, they show that the sperm with the fluorescent spot do indeed contain significantly less DNA than those without fluorescence. This optical density difference is of the order of just below 3 per cent and fits in well with the estimates of approximately 4 per cent from published linear measurement of metaphase chromosomes as the difference in length and thus presumably in DNA content between the X and the Y chromosomes. The present DNA measurements thus confirm the value of the fluorescent technique in distinguishing X and Y-bearing sperm.

In addition to the two major classes of sperm Sumner and his colleagues note

that a small proportion (1.26 per cent) have two fluorescent spots and a DNA value intermediate between the X and Y-bearing classes and conclude that these are 24,YY sperm which have arisen from Y chromosome nondisjunction at the second division of meiosis. The complementary product of such a nondisjunction would be a sperm with a haploid autosome set and no sex chromosome. These two types of abnormal gamete would, if successful in fertilization, give rise to 47,XYY and 45,X zygotes. If all the 1 per cent or so of 24,YY and a similar number of sex chromosome deficient sperm were as successful at fertilization as normal sperm, a similar proportion of both 47,XYY and 45,X zygotes might be expected. Studies of live newborn populations indicate an incidence of 0.8 per thousand live births for 47,XYY and 0.2 per thousand live births for 45,X individuals.

The XO sex chromosome complement is a very notable contribution to foetal loss (approximately 7 per cent of all spontaneous abortions), but a 47,XYY complement has not been described in an abortus. Because of the discrepancy between the proportions of presumptive 24,YY sperm and 47,XYY live births, and taking into account that there is no evidence of 47,XYY foetal loss, the authors conclude that 24,YY sperm have a reduced capacity for fertilization compared with normal sperm. This is of interest, as is the fact that there is a great excess of female 18-trisomic (47,XX,18+) newborns and also a small excess of female abortuses with this trisomy suggesting that disomic-18 Y-bearing (24,Y,18+) sperm may be at a similar disadvantage.

The authors have also studied sperm from bull, rabbit and mouse and meiotic and mitotic cells from rabbit and mouse and found no strongly fluorescing chromosome in these species.

BACTERIOPHAGES

Peaceful Coexistence

from our Cell Biology Correspondent

COLIPHAGES which peacefully coexist with, rather than kill, *Escherichia coli* cells seem to be comparatively rare—although, of course, this may well reflect nothing more significant than the selective sampling of molecular biologists—and they are comparatively poorly understood. Such phages, and fd is the most familiar, are, however, attracting increasing attention. For just as the lytic phages have proved to be ideal tools for probing many of the basic processes of gene expression—the discovery of messenger RNA and much that has followed depended on their availability—so such coexisting phages as fd may prove equally useful for probing second order biological processes. Particles of fd, for example, are apparently assembled as they pass across the bacterial cell envelope rather than in the infected cell's cytoplasm; the secretion of fd particles may well therefore be a useful model system for studying the movement of large molecules across membranes. Cells infected with fd also provide a system for investigating the continued replication of two replicons, the bacterial and viral chromosomes, in one cell.

Marvin and his colleagues (Hohn, Lechner and Marvin, *J. Mol. Biol.*, **56**, 143; 1971) have been looking at the latter problem and have come up with a model for the replication of fd, which, although similar to that proposed by Sinsheimer to account for the replication of ϕ X 174, has some unique features. The pattern of incorporation of 1 minute pulses of thymidine into fd and bacterial DNA during the first hour after infection is consistent with the model of the replication of ϕ X 174 DNA which fd DNA closely resembles. The single stranded and circular fd DNA is first converted to a closed, circular and double stranded replicative form (RF1). This, attached to some membrane site, replicates to produce progeny RF1 molecules. The model for ϕ X 174 replication envisaged that only the RF1 molecules, retaining a parental strand of DNA from the infecting particle, remain attached to membrane and able to replicate. Hohn *et al.* suggest, however, that in the case of fd replication all the RF1 molecules are able to replicate semiconservatively because they observe an exponential increase in the rate of DNA synthesis at this stage in the replication cycle. Eventually the RF1 molecules, instead of replicating semiconservatively, begin to act as templates for the asymmetric synthesis of single strands of progeny viral DNA which can be incorporated into progeny virus. Hohn *et al.* propose that this switch from double to single stranded DNA synthesis is brought about by the

product of fd gene 5, which is known to be essential for the synthesis of progeny single strands but not RF1 molecules. They suggest that this gene product somehow specifically inhibits the replication of one of the two strands of fd DNA, thereby generating single stranded molecules and preventing these from being converted into double stranded RF1 molecules.

Hohn, von Schutz and Marvin (*ibid.*, 155) have also examined what happens in cells infected and killed by fd because the secretion of progeny particles is inhibited. In such a situation, which they call abortive infection, the input fd genomes are converted to RF1 molecules but by the end of this latent period bacterial DNA synthesis, RNA synthesis, protein synthesis and ATP generation are inhibited although the synthesis of bac-

terial membrane seems to continue. The product of the fd gene 2 plays a part in this killing because fd mutants with an amber mutation in this gene do not kill *E. coli* which are prevented by one means or another from secreting progeny phage. The gene 2 product is also required for the replication of double stranded viral DNA and it is probably bound to the bacterial membrane. Hohn *et al.* suggest from all this that in abortive infection the gene 2 product interacts with the bacterial membrane in such a way as to shut off respiration, believed to be a membrane associated function, and kill the cell. Killing by fd, as well as the secretion of fd in normal infections, may therefore provide new experimental approaches to the structure and function of the bacterial envelope.

Methionine initiates Adenovirus Proteins

THIS time last year few biochemists would have readily agreed that methionine is the first amino-acid laid down at the start of synthesis of proteins in the cells of higher organisms as well as in bacteria. But in the past year it has been conclusively shown that haemoglobin, protamines in the cells of trout testis and polypeptides synthesized in an ascites cell-free system programmed with EMC virus or synthetic messenger RNAs are all initiated with a methionine residue. Methionine seems indeed to be the universal initiating amino-acid and the report by Caffier, Raskas, Parsons and Green, in next Wednesday's *Nature New Biology*, that eight or nine adenovirus proteins are initiated with this amino-acid should prove that this generalization is not over-optimistic.

Caffier *et al.* prepared cytoplasmic extracts of KB cells (a line of human carcinoma cells) infected with adenovirus type 2. These extracts support the synthesis of eight structural proteins of adenovirus particles and possibly a ninth adenovirus protein which is not part of the virion. The first amino-acid of the eight species of structural proteins, as isolated from virus particles, is either alanine or glycine but in no case is the first, N-terminal, amino-acid methionine. To test whether alanine or glycine rather than methionine are the amino-acids which actually initiate the synthesis of these proteins in their cell free system, Caffier *et al.* assayed the incorporation of methionine donated by an initiating methionine transfer RNA isolated from yeast and added to the cell free system. At least 60 per cent of the methionine incorporated into nascent adenovirus proteins, and 35 per cent of the methionine found in completed and released proteins was at the N-terminal position. Clearly in this artificial situation methionine initiator

transfer RNA from yeast can initiate the synthesis of adenovirus proteins. But is methionine the initiator in intact KB cells not supplemented with yeast transfer RNA?

To answer that question Caffier and his colleagues compared the uptake of methionine by adenovirus 2-infected KB cells exposed to a 5 minute pulse of H³ methionine and by their cell free system exposed to a 20 minute pulse of H³ methionine. In both cases, 25 per cent of all the methionine found in nascent adenovirus proteins was at the N-terminal initiating position whereas in completed and released proteins 5 per cent of the methionine was found to be N-terminal. These results strongly suggest that in KB cells adenovirus proteins are initiated with methionine. On average there are fourteen methionine residues in these eight adenovirus proteins. If the synthesis of each began with methionine and if the methionine was not cleaved from the chain until after it was completed and released, about 7 per cent of all incorporated methionine residues would be N-terminal. This is close to the observed 5 per cent, which suggests not only that all these adenovirus proteins are probably initiated with methionine but also that many of the initiating methionine residues are not cleaved until after the protein has been completely synthesized.

One other interesting detail emerges from this work; yeast initiator transfer RNA carrying a methionine residue which is formylated (with a formyl group on the amino-group of methionine) does not initiate adenovirus proteins. This result, in keeping with those of Smith and Marcker and others, indicates that it is a methionine residue, rather than an amino-acid with a blocked amino-group, which is universal to chain initiation.

GLYCOGEN BREAKDOWN

Enzyme Ensemble

from our Molecular Biology Correspondent

CHARGAFF'S deathless adage that molecular biology is merely biochemistry practised without a licence may seem to find support in comparisons with work such as that of Fischer, Krebs and others on the system of enzymes responsible for the breakdown of glycogen. What at best characterizes the thinking of the fully licensed practitioner, and is so striking a feature of this work, is the manner in which the objectives and results are related to the broad biological design, and are brought ever closer to the situation in the cell. The latest successes in this direction are described in three massive articles from Fischer's laboratory on the interrelation between the enzymes of glycogen breakdown in newly discovered subcellular particles prepared from muscle.

The breakdown of glycogen, in accordance with instantaneous energy requirements, is controlled by the activity of glycogen phosphorylase. This enzyme exists in two states: phosphorylase *b*, at least *in vivo* at high concentration, is a form of low activity, which is activated to a modest degree by AMP. Under the action of phosphorylase kinase it is phosphorylated at one serine residue in each of the four subunits, to give the highly active phosphorylase *a*. The kinase is itself activated by calcium ions, with the additional complication that a calcium-dependent protease, present in the tissue, also causes activation, perhaps adventitious, of the kinase by limited proteolysis. To complete the cycle, the *b* form is regenerated from the *a* by the action of a phosphatase, which is liable to inhibition by nucleotides.

Meyer *et al.* (*J. Biol. Chem.*, **245**, 6642; 1970) now show that all these enzymes coexist in glycogen particles, 200–300 Å in diameter, which can be prepared in several ways from muscle. The preparations also contain much larger vesicles, apparently derived from the sarcoplasmic reticulum. These can be separated from each other by sedimentation or gel filtration, and the phosphorylase and its satellite enzymes appear in the smaller glycogen particles, whereas the vesicle fraction contains highly active calcium pump ATPase.

In the second article (Heilmeyer *et al.*, *ibid.*, 6649) the mechanism of control of phosphorylase activity in these particles is examined. The phosphorylase *in situ* is entirely in the *b* form, and thus essentially inactive. The phosphorylase kinase is also dormant, but the phosphatase is active, so that no conversion to phosphorylase *a* is possible. When now magnesium ATP and calcium are added, there is a rapid and spectacular eruption of phosphorylase activity, far

too large to be put down to nucleotide activation and, as the absolute requirement for calcium ions shows, caused by the revival of the phosphorylase kinase. After an interval, depending on the ATP concentration—for this is quickly depleted by contaminating ATPase—the phosphatase regains the upper hand, and the phosphorylase activity vanishes.

In the third paper, Haschke *et al.* (*ibid.*, 6657) consider the role of phosphorylase phosphatase. They find that magnesium ATP and calcium, the very agencies responsible for unleashing the kinase, also inhibit the phosphatase. The build-up of AMP and the deamination product, IMP, which are both inhibitors of the enzyme, is altogether insufficient to account for the effect. In the absence of evidence to suggest chemical modification it seems likely that there is another inhibiting component in the glycogen particle that regulates it.

Evolving Histones?

In the past few years histone chemistry has rapidly emerged from the dark ages of not so long ago when histone chemists spent their lives arguing about each others' artefacts. It is true that the function of histones is almost as obscure as ever, but today such is the sophistication of protein chemistry that arguments now centre on the possible evolutionary relationships between histones of known amino-acid sequence rather than on how to fractionate reproducibly various types of histones. Indeed, one type of histone, fraction IV, provides the outstanding example of the evolutionary stability of a protein. Fraction IV histones of pea cell nuclei and calf thymus cell nuclei differ in sequence by only two amino-acids. How long is it since cows and peas diverged from a common ancestor? Such striking evolutionary stability is a characteristic of several types of histone from diverse sources; on the other hand there is evidence that certain histones are species and even tissue specific. Fraction V histones are the best example; these are uniquely restricted to red blood cells, but as Greenaway and Murray speculate in next Wednesday's *Nature New Biology*, fraction V histones may be ancestral to the fraction I histones of other cell types.

Greenaway and Murray noticed that the fraction V histone of chick erythrocytes can be resolved into two fractions, Va and Vb, by chromatography on 'Amberlite' columns. The two fractions, obtained reproducibly, proved to have the same N-terminal amino-acid, the same electrophoretic mobility and they do not differ in the extent to which they are acetylated, methylated or phosphorylated. In fact, after extensive tests the only difference Greenaway and

BACTERIOPHAGES

Another Enzyme from T7

by our Molecular Genetics Correspondent

DEFINING completely the functions of the chromosome of a living cell—even one comparatively so simple as a bacterium—is obviously going to take a very long time indeed. But accounting for every function coded by a viral genome may be a more practical proposition. Viruses come in many sizes and shapes, of course, and the trick of success may perhaps be to pick one with the right order of complexity. As lambdologists will ruefully vouch, even a comparatively small virus such as lambda, which has about fifty genes, has a bewildering number of control systems which are proving all too difficult to disentangle.

The very small phages have genomes which are RNA or single stranded DNA;

Murray found between the two proteins was at the position of the fifteenth amino-acid residue in their sequences. Histone Va has a glutamine residue at this position whereas histone Vb has an arginine residue.

These initial experiments were done with histones extracted from the pooled blood from about 1,000 chickens and the obvious question arose as to whether any one bird has both histone Va and Vb. Experiments with the histones from the blood of individual birds showed that they either had histone Vb or both Va and Vb. Furthermore, preliminary analyses of the inheritance of these patterns indicate that in fowl there are probably allelic genes for the two proteins. The existence of chickens homozygous for fraction Vb, however, proves that both alleles are not essential for survival.

The occurrence of such genetic polymorphism among histones increases, of course, the number of distinct histone fractions, but it reduces the complexity of their biological function because such closely related proteins are unlikely to have different functions. Indeed, as Greenaway and Murray suggest, fraction I histones, in cells other than erythrocytes, have so many properties in common with fraction V histones, restricted to red blood cells, that it is quite feasible that fraction I histones have evolved from fraction V histones. If this argument has any truth in it, it follows that fraction I histones have rendered the fraction V histones redundant in all but erythrocytes. The heterogeneity of histone fractions may well belie the range of their functions, which is probably far more restricted than the protein chemist, surveying the numerous fractions from his columns, might be tempted to predict.

the f2 group of RNA phages, for example, has only three genes, and ϕ X 174 or fd single stranded DNA phages code for about eight genes. These phages must therefore rely almost entirely on functions of their host bacterium. Phage T7, however, which has a duplex DNA genome consisting of nineteen genes, itself codes for several of the activities needed for its infectious cycle, but is not as complex as the larger phages.

This phage has already produced surprises. Gene 1 controls the expression of most of the phage genes; mutants which lack the gene 1 protein product can only make the three earliest T7 proteins. The obvious explanation seemed to be that this gene specifies a phage σ factor (as do comparable genes in the T-even phages) which directs the host cell RNA polymerase to transcribe the late genes of the phage. But T7 differs from the other phages because gene 1 proved to code for a new RNA polymerase, with a specificity for the T7 genes.

Other genes are concerned with specifying the enzymes required to replicate the phage, such as a DNA replicase and a polynucleotide ligase. Genes 3 and 6 are concerned with the degradation of host DNA which provides the nucleotides needed for the synthesis of new phages. The protein specified by gene 3 is an endonuclease which seems to attack both single stranded and double stranded DNA, and Center and Richardson report some of its properties in two articles in the *Journal of Biological Chemistry* (245, 6285, 6292; 1971).

The enzyme shows a strong preference for single stranded DNA, which it degrades about 150 times faster than duplex DNA. Its attack on duplex DNA generates single strand breaks, and it is not yet clear just how these are converted into the double strand breaks which are needed to split the DNA. And *in vitro*, at any rate, the enzyme is as active with T7 DNA as template as it is with that from the host *Escherichia coli*. How is the behaviour of the enzyme in degrading only T7 DNA *in vivo* to be reconciled with this apparent lack of discrimination? One possibility is that the product of gene 6, which also seems to be involved in degradation of host DNA, may confer some specificity on the gene 3 endonuclease. Another is that the degradation may take place so soon and so rapidly after the entry of the phage into the bacterium that only host DNA is available for attack at that time; this implies that the endonuclease must be inactivated in some way before replication of T7 DNA generates more substrates for it. At any rate, the gene 3 product has now been unambiguously identified, even if the way it works *in vivo* is not quite clear, and another gene can be ticked off on the list of those whose products are known.

The Helper and the Helped

SORTING out the relationships and interdependence of animal leukaemia and sarcoma viruses is, these days, a chief preoccupation of tumour virologists; for the genome of one RNA cancer virus can be enclosed in the envelope of, and assume, the host range of a second virus. Moreover, many tumour viruses are defective; they have become dependent on the help of a second virus in order to transform and replicate in some hosts. In next Wednesday's *Nature New Biology*, Eckner and Steeves describe just such a situation.

In 1956, Friend isolated from Swiss mice a virus preparation which, when inoculated into mice, either induces an erythroblastic leukaemia, associated with a gross enlargement of the spleen, or a lymphatic leukaemia or lymphoma associated with tumours of the thymus, the outcome of a particular inoculation depending on the strain of mice inoculated. It has since become clear that the Friend isolates contain two viruses, one of which induces lymphomas and the other induces spleen tumours or foci and erythroblastic leukaemia. But what is the relationship between these two viruses; is one a helper for the replication of the other?

Stocks of the virus which induces

spleen foci always contain the virus which induces lymphomas but the converse is not the case. Further, Eckner and Steeves found that the induction of spleen tumours in some strains of mice seems to depend on the multiple infection of the spleen cells by two or more virus particles. These two facts suggest, of course, that the virus which causes spleen foci requires the help of the lymphoma virus, for that would explain both the presence of lymphoma virus in stocks of the spleen focus inducing virus and the observation that the induction of foci depends on multiple infection. But it might be argued that multiple infection somehow impairs the immune system and as a result spleen foci are able to develop. To rule out this possibility, Eckner and Steeves treated mice with cortisol to impair their immune system and found that the induction of foci remained dependent on multiple infection. When, however, stocks of the focus inducing virus were diluted into stocks of the lymphatic leukaemia virus, the induction of foci seemed to be dependent on single infections. In this situation there is clearly a great excess of helper virus; cells are always infected by it so that the induction of foci seems to depend on a single infection by the focus forming particle.

Linkage of Retinal to Opsin

RHODOPSIN, a visual pigment found in vertebrate retinal rods, transduces light into a neural message. It is a chromoprotein and consists of 11-*cis* retinal (retinene aldehyde) and an unspecified protein, called opsin. The two are said to be linked by a Schiff base between phosphatidyl ethanolamine (PE) and retinal, which moves after exposure to light to the ϵ -amino-group of a lysine residue in the protein. Anderson, Hoffman and Hall question this assumption in next Wednesday's *Nature New Biology*. Is the N-retinylidene-phosphatidyl-ethanolamine (N-RPE) which has been extracted from rod outer segments, and which is dark adapted and then not exposed to light, associated with rhodopsin or not? N-retinyl-phosphatidyl-ethanolamine (N-RH₂PE) has also been extracted from rods after acidification of rhodopsin and the sodium borohydrate fixation of retinal to its original site by a secondary linkage. Anderson *et al.* stress that the extracts used contain much phospholipid and retinal not bound to opsin, and they suggest that the isolation of N-RPE may be derived instead from a source other than the retinal-opsin link.

To test if this is so, they measured the turnover of the rhodopsin in the outer segment disks which form part of the rods. They injected frogs with labelled

³H-retinol and then measured the radioactivity three days later from suspensions of their rod outer segments, subdivided into three groups, A, B and C. A was acidified, treated with sodium borohydrate, and was then subdivided into aqueous and lyophilized subgroups. Lipid was extracted from the aqueous subgroup by treatment with a 2:1 chloroform-methanol mixture: the separated protein contained 73 per cent of the total radioactivity. The lyophilized subgroup, which had been extracted similarly but without protein partitioning, retained 82 per cent of the activity in the protein. It was found that all the radioactive part which had been removed from the rhodopsin was associated with free retinol, and that no tritium exchange had occurred between it and opsin.

Unlike groups A and B, group C contained rod outer segments not originally purified on an 'Agarose' column. C was subdivided, one half being treated in the same way as A, the other like B; less than 40 per cent of the total radioactivity was associated with the protein and an average of 30 per cent was recovered with N-RH₂PE. Anderson *et al.* thus confirm the presence of N-RPE in cetyltrimethylammonium bromide solutions of rod segments, but demonstrate that this lipid forms no part of the rhodopsin chromophore.

Marriage and Fertility in Academic Life

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An analysis of a sample of entries in the 1969 edition of *Who's Who*, suggests that male arts specialists are nearly five times as likely as scientists to remain single.

It has been suggested^{1,2} that specialists in the arts and in biological and physical sciences differ not merely intellectually but in personality, and that students perceive these professional groups in the light of simple, highly stereotyped preconceptions³. These studies imply that adult specialists in the arts lead relatively uninhibited and unconventional personal lives; that biologists are more conventional, and that physical scientists are more conventional still. The more prosaic and quantifiable aspects of such individuals' personal lives, such as, for example, their patterns of marriage and fertility, have, however, been little studied. Pertinent sources of biographical information^{4,5} have also been neglected.

One such source of information is the publication *Who's Who*⁶. This lists, among others, men eminent in British academic life. Fellows of the Royal Society and the British Academy, for example, and professors at Oxford and Cambridge, all receive invitations as a matter of course and few distinguished scholars or scientists are omitted.

Entries in *Who's Who* are completed by the individual concerned, and normally but not invariably include the following information: date of birth, date of marriage(s), number of children and an indication of whether an earlier marriage ended in death or divorce. Details of school and university education, publications, and appointments held are also included. As a biographical source, *Who's Who* is imperfect, but its accuracy bears comparison with responses to interviews or questionnaires, and it offers a rate of response that no other source can rival.

We studied a sample of individuals in *Who's Who* consisting of all those males in the 1969 edition, classified into the following academic groups, who were born between 1900 and 1925, and who had been educated substantially in the United Kingdom. The arts group came from the following fields: philosophy ($n=42$), classics ($n=61$), history ($n=83$) and English literature ($n=30$). The biological science group was drawn from botany ($n=45$), zoology ($n=55$), physiology ($n=20$), genetics ($n=15$), cell and microbiology ($n=12$). The physical scientists came from physics ($n=93$), chemistry ($n=77$), metallurgy ($n=19$), geology and mineralogy ($n=31$) and engineering ($n=109$). The engineers were restricted to those who held senior academic posts, or who were Fellows of the Royal Society. Most of the individuals in each of the three academic groups were professors in British universities and their average age was 57. Ninety-three per cent were married; and of these, 68% had been married for at least 25 years and 94% for at least 15 years.

Table 1 gives the percentages in each of the three academic groups who were single or who had childless marriages. The differences between the three groups are unmistakable. The arts specialists are nearly five times as likely as the scientists to remain single. They are also the most likely to have childless marriages, the tendency, for one reason or the other, to remain childless being particularly marked among classicists (41%). The differences between biological and physical scientists are less marked. Both groups had married

in all but a few cases; but the physical scientists are nearly twice as likely as the biologists to have a childless marriage.

These differences in childlessness influence the mean overall fertility rates for the three academic groups: members of the arts group had on average 1.83 children, the biologists 2.50, the physical scientists 2.05. These rates alter relatively little, however, if the groups are restricted to men who have experienced at least 15 years of uninterrupted marriage (2.16, 2.52 and 2.12 respectively).

Table 2 gives the percentages in the arts, biological sciences and physical sciences who married late (age 35 or later) or who have divorced. From these figures, the arts specialists seem to be the group most likely to marry late; half again as likely as the biologists, more than twice as likely as the physical scientists. The pattern for divorce is different. The highest rate was found among the biological scientists: they seem to be three and a half times as likely to divorce as physical scientists, and more than twice as likely as the arts group. In all three groups, divorcees had, on average, more children than others (arts group, 2.70; biologists, 3.05; and physical scientists, 2.45); and in the arts and physical sciences, but not in biology, those married late seemed less fertile (arts group, 1.24; biologists, 2.57; physical scientists, 1.64).

With regard to late marriage and divorce, the arts and biological science groups are each reasonably homogeneous. The physical scientists, on the other hand, contained one obviously discrepant group—the physicists. When compared with chemists, for example, they seem to be six times as likely to divorce. If the physicists are excluded from the sample of physical scientists shown in Table 2, leaving it predominantly a group of chemists and engineers, the physical science divorce rate drops to 1.7%.

It is also interesting that mathematicians ($n=59$, omitted from Tables 1 and 2) differ from all the scientific groups. Their divorce rate seems moderate (3.8%) and their likelihood

Table 1 Proportions of Eminent Men in the Arts, Biological Sciences and Physical Sciences who remain Childless

	Single	Childless marriage	Total
Arts $n=216$	(32) 14.8%	(35) 16.2%	(67) 31.0%
Biological sciences $n=147$	(3) 2.0%	(9) 6.1%	(12) 8.1%
Physical sciences $n=329$	(12) 3.6%	(38) 11.5%	(50) 15.1%

The source of this information ($n=692$) was ref. 6. Frequencies in each of the three columns represent significant deviations from chance: χ^2 test, $P<0.001$, 0.025, 0.001 respectively.

Table 2 Proportions of Eminent Men in the Arts, Biological Sciences and Physical Sciences who Marry Late (35+) and who Divorce

	Marry late	Divorce
Arts $n=216$	(29) 13.4%	(10) 4.6%
Biological sciences $n=147$	(14) 9.5%	(18) 12.2%
Physical sciences $n=329$	(18) 5.5%	(11) 3.3%

The source of this information ($n=692$) was ref. 6. Frequencies in both columns represent significant deviations from chance: χ^2 test, $P<0.01$, 0.001 respectively.

of remaining single seems quite high (10.2%) a pattern that identifies them more nearly with the arts group than any other. The social scientists ($n=30$) were another distinctive group omitted from our analysis. A small and by no means homogeneous sample of psychologists ($n=18$), sociologists ($n=5$) and social anthropologists ($n=7$), they are distinguished from other scientists in the study by their high divorce rate (23.3%).

Such evidence, of course, sheds no light on causes; it can as easily be interpreted from biological, psychological, or social points of view. But simple explanations, either in terms of social class or of the biased composition of the *Who's Who* sample, find little support from the data. Although the arts, biological science and physical science groups came in differing proportions from Headmasters' Conference schools (65%, 57% and 37% respectively), and from the Universities of Oxford and Cambridge (74%, 52% and 34%), there seems to be, with one exception, no significant interaction between either factor and the patterns of marriage and fertility within each academic group. The exception lies in divorce among biologists. Those from Headmasters' Conference schools seem more than five times as likely to divorce as their colleagues from grammar schools (19.2% as against 3.6%; χ^2 test, $P<0.025$).

Nor can the results be explained in terms of differences between the academic groups in the number of years they have been married. Although the average ages of the arts, biological science and physical science groups differ slightly (58.1, 59.1 and 56.7 respectively), the length of time since first marriage does not differ significantly between them (χ^2 test, $P>0.1$). Moreover, in science at least, marriage and fertility patterns have no bearing on the level of professional success an individual achieves. If the samples of scientists are restricted to those who are Fellows of the Royal Society, the patterns shown in the bottom two rows of Tables 1 and 2 are not significantly changed. This result supports my earlier findings that the differences between academic fields are easier to predict than success within them¹.

The data summarized here help to substantiate the links between the intellectual realm and those of personality and style of life. Each of the three academic groups seems to have its distinctive pattern. Arts specialists are the most likely to remain single; and if they marry, to do so late and to remain childless. Most scientists seem to marry. Biologists differ from physical scientists in that they are the more likely to marry late, to have large families, and to become divorced.

Broadly, these findings are in keeping with earlier research on the recruitment of scientists, and students' perceptions of them. Not even the discrepant marital patterns of physicists, nor the similarities of mathematicians to the arts specialists are entirely unexpected. Results for the arts specialists conform less well. The high rates for remaining single, for childless marriage and late marriage, and the low rate for divorce are all at variance, superficially at least, both with students' perceptions of the arts and with evidence about the type of student which the arts faculties attract. An interesting complement may be found in the personal lives of novelists, poets and playwrights. The sample of such writers in *Who's Who* is catholic; but a preliminary analysis of the most distinguished suggests a pattern analogous to that of scholars in the arts in all respects but one—divorce. Among creative writers this is very frequent indeed.

Clearly, such results as these cannot form a basis for hasty generalization. The men studied are the eminent few and not necessarily representative of their specialities as a whole—patterns of recruitment, as well as of marriage and fertility, may prove to vary from one country to another, and even from one generation to the next within a given discipline. It is also possible that error has occurred at source, in the shape of omissions from the individual entries in *Who's Who*.

¹ Hudson, L., *Contrary Imaginations* (Methuen, London, 1966).

² Hudson, L., *Frames of Mind* (Methuen, London, 1968).

³ Hudson, L., *Nature*, 213, 228 (1967).

⁴ Galton, F., *Hereditary Genius* (Macmillan, London, 1869).

⁵ Webb, J. E., et al., *Unobtrusive Measures: Non-reactive Research in the Social Sciences* (Rand McNally, New York, 1966).

⁶ *Who's Who* (Black, London, 1969).

Pozzuoli Event in 1970

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A crustal upheaval near Naples in March 1970 was unusual in not being accompanied by noticeable earthquakes. This could be interpreted in terms of the visco-elasticity of the Earth's crust.

At Serapeo, on the Bay of Pozzuoli, near Naples, three marble columns, said to be the remains of a Roman temple, provide a record of movements of the Earth's crust since the second century BC. According to Parascandola¹, the floor at Serapeo has subsided by about 11 mm per year (Fig. 1), and been raised several times by calamities. These included the Campanian earthquake in AD 63; the eruption of Vesuvius in AD 79; a mud eruption at Solfatara in 1198; an eruption of Arso on Ischia in 1302; earthquakes felt at Pozzuoli in 1416 and 1488, and in 1536–38, earthquakes followed by the eruption of Monte Nuovo. In Italy crustal movements of this sort have been known as *bradisimi* (slow oscillations) since the nineteenth century. Recently Oliveri and

Quagliariello² presented a theory of origin of the *bradisimi* at Pozzuoli, interpreting the subsidences as self-loading compactions and the upheavals as variations in the flow of ground water filling porous pyroclastics.

In early 1970, a conspicuous upheaval was noticed at a zone centred on Pozzuoli. At the end of February 1970 some old stone walls at Pozzuoli were cracked by the upheaval and the steaming area of Solfatara increased.

Campi flegrei (fiery fields, Fig. 2) behind Pozzuoli are full of volcanoes, craters, hot springs and steaming fields. The oldest eruption centre which has been dated is Astroni Crater, which erupted about 1500 BC. Next come Fossa Lupara, Concola, Fondo Riccio and Monte Nuovo. In the light of this history of volcanism further eruption might be expected around Pozzuoli.

The most recent event was an anomalous upheaval in March 1970. Changes in height of bench marks around Pozzuoli between 1953 and March 1970 (Fig. 2) show that the maximum upheaval amounted to about 90 cm, assuming that the easternmost point, about 4 km from Pozzuoli, was unchanged. The uplifted zone was circular, centred on Pozzuoli. The upheaval probably began in October 1969.

It is remarkable that no earthquakes were felt at Pozzuoli

during the upheaval. Since the end of February 1970 teams from the Institute of Geophysics of the University of Naples and the Vesuvian Observatory have been making seismic measurements in three places at and around Pozzuoli. Usually a few micro-earthquakes of magnitude 0–2 and $S-P$ duration less than 1 s were registered each day. This seems to be remarkably little activity for a time when an anomalous upheaval was in progress, but we have no precise data about normal seismicity there. Earthquake swarms in Japan, however, have been accompanied by crustal movements. The absence of earthquakes in this case could be explained if the upheaval were due to the visco-elastic properties of the Earth's crust. If the upper part of the crust is visco-elastic, one can expect the following two stages: the first when deformation is proportional to the frequency of earthquakes, and the second when there are no earthquakes. The Pozzuoli event may be an example of the latter stage.

The observed upheaval at Pozzuoli can be interpreted by neither of two theoretical curves (Fig. 3) which assume an elastic crust. The curves represent the deformations of a semi-infinite elastic body due to a stress origin buried at a depth of 2 km. Pressure distribution is expressed in spherical harmonics $P_n^m(\cos \theta)$. The observed deformation must be plastic, not elastic.

The distribution of Bouguer gravity anomalies in this region (Fig. 4) shows that a low anomaly of 7–8 mgal

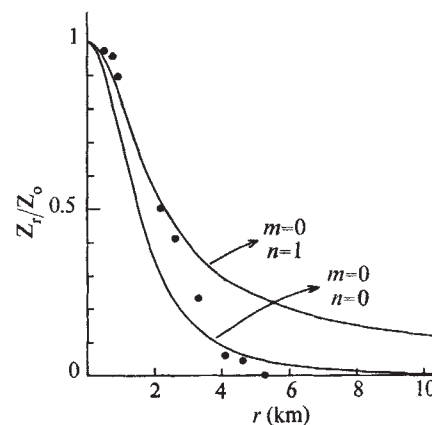


Fig. 3 Relative deformation of surface of elastic body due to a stress origin buried at a depth of 2 km. Solid circles denote the values observed at Pozzuoli ($Z_0 = 85.7$ cm).

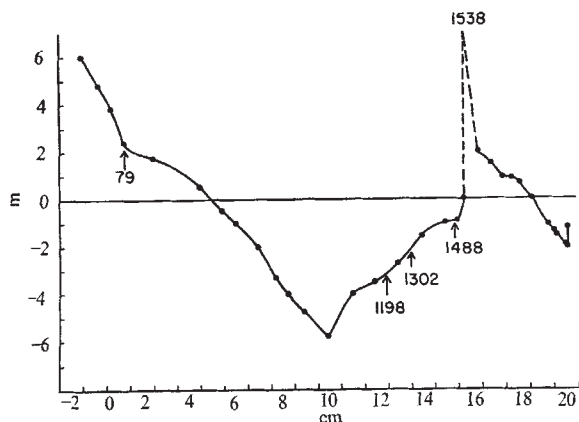


Fig. 1 Changes in height of the floor of Serapeo after A. Parascandola.

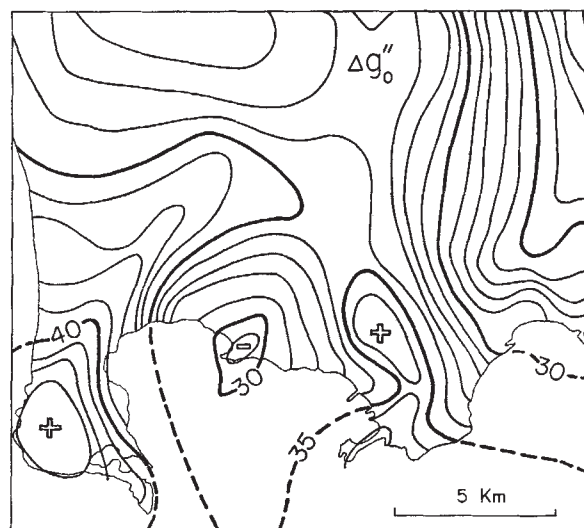


Fig. 4 Distribution of the Bouguer gravity anomalies in mgal., after the Geological Survey of Italy.

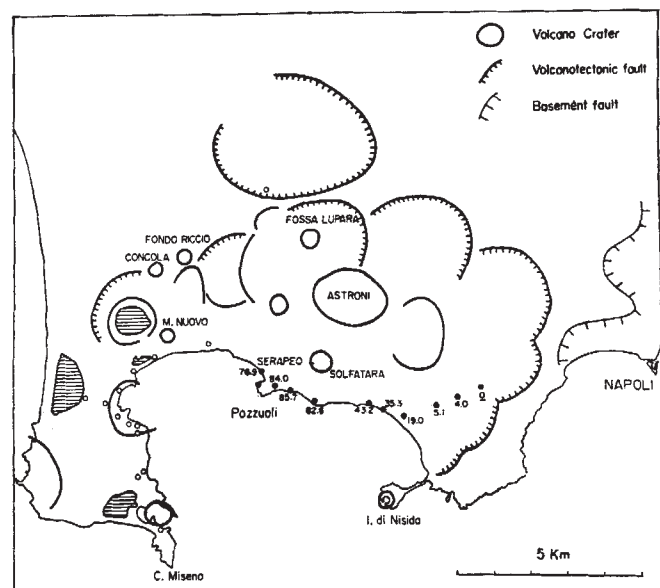


Fig. 2 Campi flegrei. Solid and hollow circles denote bench marks for precise levels. Numerals denote the changes in height during the period 1953 to March 1970, after the Provveditorato Opere Pubbliche di Napoli. The unit used is the centimetre.

coincides with the centre of the upheaval at Pozzuoli. This may be caused by light deposits (volcanic tuffs) 1–2 km deep at the centre. These deposits would subside continuously as a result of compaction and rise through plasticity, by reacting with hot volcanic material.

According to G. Imbò (personal communication), the phenomena continued slowly after March 1970. The bench mark at the harbour master's office at Pozzuoli rose 14.8 cm between March 1 and June 11, and Nisida Island rose 2.7 cm between March 21 and June 9. This means that a slightly larger area is associated with the *bradisismi* than had been assumed. The seismometers at Pozzuoli registered 256 micro-earthquakes between March 1 and June 10. Almost all were very small, although a few were registered as III or IV on the Mercalli intensity scale.

In conclusion, the rapid upheaval at Pozzuoli, not accompanied by any conspicuous shocks, can be interpreted as a phase of visco-elastic activity in the upper crustal material. Volcanic tuffs would have been affected by some volcanic reactions, such as intrusion of magma or steam. This interpretation does not contrast with the theory of Oliveri and Quagliariello².

I thank the Provveditorato Pubbliche in Naples for access to valuable data.

¹ Parascandola, A., *I Fenomeni Bradisismici del Serapeo di Pozzuoli* (Genovese, Naples, 1947).

² Oliveri del Castillo, A., and Quagliariello, M. T., *Sulla Genesi del Bradisismo Flegreo* (Atti Ass. Geof. It., XVIII Conv., Naples, 1969).

Uses of Artificial Insemination

by

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Techniques for semen storage and artificial insemination of animals have developed considerably during the past twenty-five years but biological, social and economic factors are still limiting the full development of this technology.

EARLY examples of extra-coital insemination exist in mythology and legend from times when the function of coitus was not understood. For example, Heape¹ referred to a fourteenth century story of an Arab who successfully inseminated his own mare with semen collected from a stallion owned by a neighbouring hostile tribe. But credit for the conclusive successful demonstration of artificial insemination of mammals is due to Spallanzani², an Italian priest who worked in the latter part of the eighteenth century. He reported the birth of three puppies after the insemination of a bitch "... artificially in the following manner. A young dog of the same breed furnished (him), by a spontaneous emission, with nineteen grains of seed, which were immediately injected into the matrix, by means of a small syringe introduced into the vagina".

Although Spallanzani's experiments were recognized when he did them, little attempt was made to use the technique until early in the twentieth century when a Russian³ applied it to mares. After about 1930 it was used with other farm animals and gradually large scale use developed, until the Second World War, after which expansion was rapid. A census during the last decade⁴ showed that in one year 59 million cows, 47 million ewes, 1 million sows, 125,000 mares and 56,000 goats were artificially inseminated. Other mammals have been inseminated in fewer numbers (including the domestic dog and cat, water buffalo, alpacas, laboratory rodents, rabbits and so on) and the technique has been applied successfully to birds (for example, 4 million turkey hens inseminated per year)⁴, fishes, amphibians and insects. Artificial insemination is used most in the more economically advanced regions and in some countries it is applied to 99 per cent of dairy cows.

The present application of artificial insemination, however, can be misleading, for it has been used for very few of more than 4,000 species of mammals existing and, because successful methods for prolonged storage of semen have only been developed for the rabbit and the domestic cow, it is of limited use for most of those species to which it is currently applied. In this review I shall consider briefly the current methods for artificially inseminating mammals, the problems involved and the future use of the technique. For more detailed descriptions of methods the reader is referred to some⁵⁻⁸ of the numerous reviews and textbooks available.

So far no harmful effects have been demonstrated, on present or succeeding generations, from the use of preserved semen or artificial insemination. Of course, it must be applied with considerable caution to avoid the development or spread of hereditary faults including sub-fertility. These are some of the advantages of the use of artificial insemination. (1) In the production of livestock it can increase the rate of

genetic improvement by expediting progeny testing of males and then increasing the use of superior sires. Its use with dairy cattle in Japan between 1939 and 1962 was associated with an increase in the country's milk production per cow from 2,700 to 4,840 kg⁴. (2) Artificial insemination makes possible better use of crossbreeding livestock. For example, with pigs, it is possible to obtain heterosis to improve grade livestock, to change the form of production—say, from wool to meat producing sheep. With fur producing animals, it is possible to vary coat colour according to fashion and to facilitate the breeding of animals of such different size that natural mating would be difficult, for example the Shire horse and Shetland pony or the great dane and pekinese dogs. (3) Artificial insemination permits hybridization between "species" which would not normally mate or do so only rarely; for example, the fowl and pheasant have been crossed⁹. (4) In veterinary and medical practice artificial insemination facilitates the use of incapacitated or oligospermic males. Banks of deep frozen semen can be used in case of death, and for humans they have been proposed as an assurance against the hazards of war and its consequences, vasectomy and other factors that may affect fertility or the capacity to copulate. (5) Between zoos it would often be preferable, or only possible, to buy semen rather than borrow or buy scarce males and the establishment of semen banks would provide an insurance against the extinction of animal species. (6) The use of artificial insemination is often cheaper and certainly less hazardous than keeping or transporting some large male animals and this is a reason for its rapid acceptance by dairy farmers. (7) Artificial insemination has been used effectively to prevent the transmission of infectious venereal diseases and, for example, was practised in Rumania until 1961 solely to eradicate dourine from the horse⁴. (8) The physiologist finds artificial insemination a valuable tool. It may be used to determine the number of spermatozoa required for fertilization, the correct timing of insemination, comparisons of the fertility of spermatozoa from different males, and many other factors.

Collection of Semen

Semen is usually collected from animals by training the male to serve an artificial vagina⁵ or by stimulating ejaculation with an electric current¹⁰. The success of either method depends on the operator, the preparation of the male and the equipment used. These factors probably account for any differences in the quality of semen collected by either method. Other methods of collection include the injection of drugs¹¹ to induce ejaculation and masturbation and, if all else is unsatisfactory, the recovery of spermatozoa from the male reproductive tract after slaughter.

The semen of animals¹² consists primarily of spermatozoa and seminal plasma. The numbers of the former and the volume and composition of the latter vary greatly within and between species (Table 1); between individuals of a species they may be affected by such factors as those already stated, frequency of collection and season.

Seminal fluid is a mixture of secretions from the male accessory organs of reproduction (Fig. 1) and differences in volume and composition between species of animals are explained by the possession of varying combinations and sizes of

Table 1 Some Values for the Collection, Storage and Characteristics of Semen

Animal	Quantity per ejaculate			No. of ejaculates per week	Storage of semen		
	Volume (ml.)	No. of sperm $\times 10^6$	No. of inseminations		Rate of dilution	Temperature (°C)	Duration
Cattle	4	4,000	400	4	1:100	-196	Many years
Rabbit	1	150	20	7	1:10	-196	Many years
Man*	3.5	350	2	4	1:1	-196	Many years
Goat*	1	3,000	60	14	1:4	-196	Many years
Sheep*	1	3,000	60	14	1:4	5	2 days
Horse*	70	8,400	5	3	1:2	5	2 days
Dog	9	2,700	15	3	1:4	5	2 days
Pig	250	40,000	30	3	1:5	15	3 days
Guinea-pig	0.5	13	1	2	1:2	20	2 h

Values are estimates after examination of the literature. They are based on the most extensive use of semen rather than the commonest methods in current use and are given only as an indication. In general, fewer spermatozoa are inseminated for semen stored at 5° C than samples deep frozen. Temperature and duration of semen storage refer to conditions that may be expected to give longest storage and ensure satisfactory pregnancy rates (about 60%) after artificial insemination.

* Several inseminations of semen that was deep frozen are usually required to obtain good conception rates; even so, results have been variable.

some of the glands. During ejaculation separate glands may, to varying degrees, secrete in order (for example, particularly so in the boar, dog and stallion but just detectably in the bull and man) so that an ejaculate may consist of one or several distinct fractions usually before and after a sperm rich fraction.

When possible, only the sperm rich fraction is collected for dilution, for seminal plasma is usually a poor medium for storing semen, and fractions of the semen of some animals

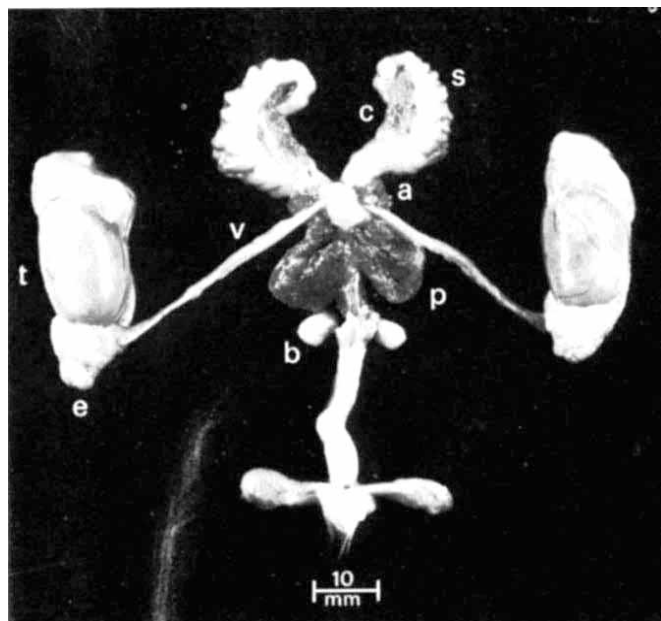


Fig. 1 Reproductive tract of male rat dissected to show the principal accessory organs. a, Ampullary glands; b, bulbourethral glands; c, coagulating glands; e, epididymidis; p, prostate glands; s, seminal vesicles; t, testis; v, vasa deferentia. Secretions from the glands and seminal vesicles constitute most of the seminal plasma. Secretions from the coagulating glands cause coagulation of semen to form a seminal plug.

gelatinize or cause coagulation. Thus, during ejaculation of the boar, for example, most of the spermatozoa are collected before the last, gelatinous fraction is emitted. But the coagulation of semen from rodents and some other animals remains a problem as it is not possible separately to collect the secretions of the glands that cause the formation of a hard rubbery mass (the seminal plug) from which spermatozoa cannot be separ-

ated. Surgical removal of the glands has been demonstrated¹³, but it is time consuming and not generally practised.

The frequency with which semen can be collected from males varies greatly between species (Table 1). In the short term the reserves of spermatozoa in the epididymis can be exploited, but for continued collection the rate is limited by the production of spermatozoa in the testes. This varies between animals, according to the size of the testes and other factors. The bull and the ram have been estimated¹⁴ to produce about 7×10^9 spermatozoa per day.

Evaluation and Preservation

A major difficulty in the application of artificial insemination and the storage of semen is the absence of a single or even a combination of criteria for predicting the fertility of a sample of semen. A relationship, of limited predictive value, between physical activity and fertility¹⁵ is used for practical purposes and involves simple microscopic methods of estimating the number of living spermatozoa and their individual activity. The use of these methods has so far survived the development of numerous sophisticated devices involving photo-multipliers, a television scanner, cinematography and an impedance bridge.

Because spermatozoa are overcrowded in semen collected from most animals, samples must be diluted for storage. Diluents contain a metabolic substrate (usually a sugar) and electrolytes must be used in concentrations to account for the sensitivity of spermatozoa to changes in pH and osmotic pressure^{16,17}. Milk¹⁸ and egg yolk¹⁹ or both are also included because of the protection afforded by their high molecular weight constituents against the damaging effects of cooling ("cold shock")²⁰ and dilution^{16,21,22}. For frozen storage, glycerol²³ or dimethyl sulphoxide²⁴ must also be included to protect against the damage incurred during freezing or thawing. Further, antimicrobials^{25,26} may be used to reduce the growth of organisms or the transmission of venereal diseases.

There have been numerous reports of poor results after the use of milk or egg yolk in diluents²⁷, and other natural products, such as tomato and coconut juice, have been used. None of the substitutes tested, however, is completely satisfactory either in the amount of protection afforded or the consistency of results. Unfortunately, much of the research into diluent composition has been of a very applied nature and there is still a need to define the specific chemical reagents that protect spermatozoa during various stages of processing²⁸.

There is a reduction in activity of spermatozoa as their temperature is decreased, and so the principal approach to long term preservation has been to store semen at low temperatures. Methods of preparing deep frozen semen are an extension of methods used to store semen at higher temperatures. A standard technique for deep freezing bull semen is to dilute freshly collected samples twenty to forty-fold with buffered egg yolk and cool to 5° C for one to three hours. Then it is further diluted 1:1 with a buffered glycerol solution (preferably containing a sugar²⁹), stored for up to eighteen hours "to equilibrate", cooled to the freezing point of the eutectic mixture (about -12° C) at a rate of 1° C min⁻¹, cooled to -40° C at 3° C min⁻¹, and then transferred to refrigerators at the temperature of solid carbon dioxide (-79° C) or liquid nitrogen (-196° C). The type of diluent, rate of dilution and processing times are inter-related factors affecting the survival of spermatozoa so that, as may be expected, several quite different methods of freezing semen have been developed. These include two which may have economic advantages: freezing drops of diluted semen on dry ice³⁰ or cooling samples in liquid nitrogen vapour³¹. With the latter method samples may be contained in plastic straws that can be used as part of the inseminating pipette³².

The detrimental effects of high dilution and "cold shock" vary in magnitude between species and are important factors limiting semen preservation. It is now possible to freeze bull semen without reducing the chance of pregnancy after a

single insemination³³. Encouraging results have also been obtained with deep frozen rabbit semen³⁴. More than five-fold dilution, however, may reduce the fertility of ram semen, and cooling to 5° C causes a further reduction and only about 20% lambing can be expected after one insemination of deep frozen samples³⁵. Poor or variable results have also been obtained with human, stallion and goat semen and there are no authentic reports of fertility of deep frozen boar or dog semen.

A reduction of viability and change in structure of spermatozoa^{36,42} are usually associated with this reduction of fertility, and although these changes may not be highly indicative of fertility changes they are considered to indicate the importance of obtaining more viable spermatozoa after storage.

Detection of Oestrus

A major factor limiting the practice of artificial insemination is an incomplete knowledge of the reproductive physiology of the female. Because spermatozoa may have to spend a period in the female reproductive tract before acquiring the ability to fertilize^{43,44} (that is, they have to capacitate) insemination must occur before ovulation. But because processed spermatozoa may have reduced viability their time in the female tract must be minimized.

The method used to detect ovulation depends on the reproductive pattern of the female. In some animals (rabbits, camelids and some mustelids) ovulation is induced by mating which may occur at any time during the breeding season. Ovulation can be induced in this type of animal by mating with a vasectomized male or injecting gonadotrophins.

In most animals, however, ovulation occurs spontaneously either near to or at the end of an oestrous (heat) period, or at about mid-cycle in menstruating animals. Injection of hormones can also induce ovulation in these animals, but only at certain times of the cycle. Indeed, except for man (and possibly some of the great apes) the female only accepts the male during oestrous periods. But because oestrus is a behavioural phenomenon and is not overtly displayed in many animals it is often difficult to detect. Methods of detecting oestrus include observation of behavioural activity of the female, the use of vasectomized males either carrying crayons that mark the female during mating or that leave a seminal plug in the vagina (for example, rodents) and daily inspection to detect cytological changes of the vagina or morphological changes of the external genitalia. Clearly it is advantageous to know and handle animals individually and this must be an important reason for the early success of artificial insemination of dairy cattle compared with animals (such as sheep), kept less intensively and in large flocks. For both technical and management reasons there is considerable demand for a method that will bring a large group of females into oestrus followed by ovulation at a precisely predetermined time. Some success along these lines has been obtained with cattle⁴⁶, sheep⁴⁷ and pigs⁴⁸ by administering a substance that inhibits ovulation (usually a progestagen) to the flock for a certain period and withdrawing treatment at a predetermined time. Oestrus subsequently occurs over several days, and the time of ovulation can be controlled more precisely by injection of a gonadotrophin. Unfortunately, this method has been of limited value because conception rates are low at the first oestrus after withdrawal and synchronization is poor at the next oestrus.

When ovulation time has proved difficult to predict, good fertility has often been obtained by inseminating the female at intervals near the expected time of ovulation. Insemination may also be done during several consecutive oestrus periods. Reports of reasonable to good pregnancy rates after artificial insemination of deep frozen human⁴⁹, stallion⁵⁰, goat⁵¹ and ram⁵² semen can probably be explained largely as a consequence of repeated inseminations of the female. But this "shot-gun" approach really evades the problems and should be considered an intermediate measure during the development of suitable insemination techniques. The

unstated use of these methods is probably a reason for inconsistent reports in the literature on the fertility of stored semen.

Method of Insemination

Cows can be inseminated artificially by guiding a pipette, loaded with spermatozoa in 0.5–1.0 ml. of fluid, through the lumen of the vagina and cervix into the uterus and expelling the contents into the uterine horns (Fig. 2). Methods of preparing and inseminating semen, however, must be varied according to the structure of the female reproductive tract.

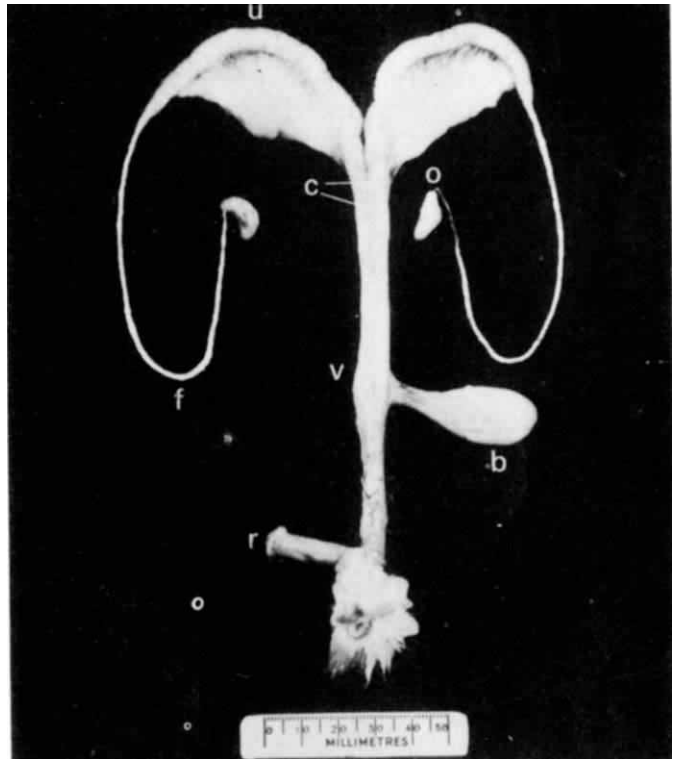


Fig. 2 Reproductive tract of female rabbit dissected to show: b, bladder; c, cervix; f, fallopian tube; o, ovary; r, rectum; u, uterine horn; v, vagina. The vagina of the rabbit is particularly long and is joined to the separated uterine horns by two cervical canals. Does are artificially inseminated by depositing semen samples at the anterior end of the vagina so that spermatozoa may penetrate both cervixes.

Embryologically the tract develops from the paired Müllerian ducts, which differ among animals in the amount of development and fusion of the vaginae, cervical canals and uteri (Fig. 2); from the duckbilled platypus in which the full length of the tract is paired, to humans in which the tract is singular, proximal to the fallopian tubes. Thus, depending on species, semen must be deposited into one or two vaginae, cervixes or uterine horns to ensure that spermatozoa reach both fallopian tubes. Further, as the wall of the cervix of some animals (such as the ewe) is deeply folded it limits penetration of the insemination pipette.

The number of spermatozoa (Fig. 3) and the volume of fluid inseminated are also important factors. At least 50 ml. of fluid must be used to inseminate a sow but less than 0.2 ml. is needed for a ewe. A factor which limits the dilution of ram semen is the difficulty of inseminating fluid into the cervix of the ewe^{35,53}, and the problem can be avoided by concentrating the semen before insemination by centrifuging and removing excess fluid.

The importance of the male has been too readily overlooked by many technologists practising artificial insemination. The seminal plug formed by the semen of many rodents and some other animals may not be necessary for good fertility after natural mating, but it could be useful after artificial insemination to ensure that spermatozoa are not lost from

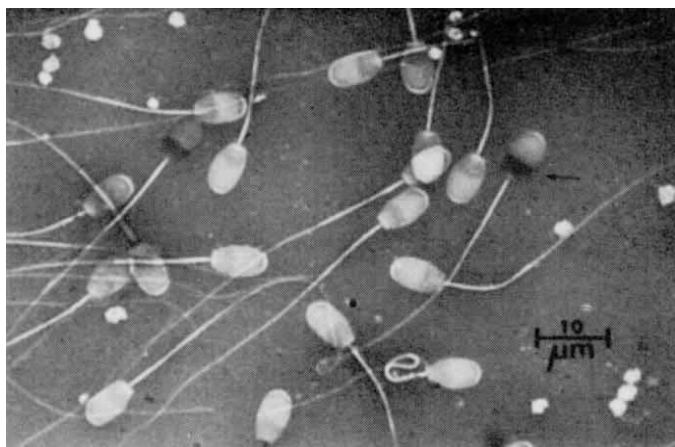


Fig. 3 Photomicrograph of an eosin-nigrosin smear of ram semen. The staining reaction of eosin is commonly used in semen evaluation; spermatozoa stained with the dye (arrow) are considered "dead".

the female reproductive tract. Indeed, although human semen does not form a plug (but does gelatinize for a short time) it is recommended⁴⁹ that a cervical cap be used when inseminating women.

It has already been mentioned that coitus induces ovulation in some animals and must be accounted for during a programme of artificial insemination. Furthermore, when inseminating the laboratory rat or mouse the stimulation of the cervix by the male during coitus must also be substituted to ensure that a functional corpus luteum is formed and that the uterus is prepared for implantation of the embryo. Also, the effect of mating on the release of oxytocin from the posterior pituitary and the importance of this and the oxytocic substance in semen on transport of spermatozoa through the female reproductive tract are poorly understood. Certainly it has been shown that post-insemination coitus is beneficial in sheep⁵⁴.

The presence of the male, without any contact, may also be important⁵⁵, for as well as affecting behavioural activity of several animals, pheromones, by chemical communication, may be necessary to maintain pregnancy and cyclic activity of some rodents.

Future of Artificial Insemination

The future application of artificial insemination depends largely on improvements in methods of detecting oestrus and ovulation and of semen collection, evaluation, preservation and insemination. Many of these will undoubtedly come as by-products of an increased knowledge of the physiology of reproduction. Nevertheless, the development of such methods as electro-ejaculation and the use of glycerol indicate the value of research orientated towards application.

The future of artificial insemination also depends on other technological developments. Those that would complement the technique and increase its use are development of methods to separate spermatozoa according to fertilizing capacity, the possession of sex determining chromosomes or the absence of abnormal chromosomes or chromosomes carrying "lethal" genes. Alternatively, if it proves practicable to transfer ova or embryos to foster mothers and to develop suitable methods of superovulating females, fertilizing ova *in vitro* and deep freezing ova or embryos, their use might, to some degree, supersede that of artificial insemination.

At present there is a considerable demand to improve and expand the application of artificial insemination of domestic animals. Indeed, improvements of economic conditions in underdeveloped countries alone will be associated with its use to up-grade farm animals. Its increased use with man seems probable at least for therapeutic reasons, as in cases of oligospermia. And changes in world attitude may ensure that semen preservation and artificial insemination will play a part in the

preservation of wild animals. But regardless of future developments of countries and techniques, artificial insemination will be used for some time as a research tool.

I thank Dr I. W. Rowlands for helpful advice and criticism and Mr T. J. Dennett for the photography.

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Structure and Evolution of the Kenya Rift Valley

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Geological evidence makes possible a reconstruction of events since Miocene times, with about 10 km of crustal separation and the pressure beneath the central rift of an upward intrusion from the mantle.

THE Kenya rift valley is one of the better known parts of the eastern rift system of Africa¹, which extends from north Tanzania through Kenya and Ethiopia to join the Red Sea and Gulf of Aden rifts at the Afar triple junction (Fig. 1). The axial Sheba ridge of the Gulf of Aden² is continuous with the Carlsberg ridge of the NW Indian Ocean³, so that the eastern rift of Africa is a continental extension of the world rift system—an interpretation which is reinforced by studies of the seismicity⁴ and plate tectonics⁵ of the Afro-Arabian region. The purpose of this article is to summarize modern geological knowledge of the Kenya rift and to reconcile this with crustal models and kinematic concepts derived primarily from geophysical data.

Epeirogenic Movements

The Kenya domal uplift is a local culmination on the eastern rim of the East African plateau. It is elliptical in plan and about 1,000 km wide. Studies of the shape and height of well preserved erosion surfaces of Miocene and late Pliocene ages provide evidence for three main phases of epeirogeny and crustal flexuring, consisting of periodic up-arching of central Kenya and local downwarping of the coastal zone⁶. Early Miocene monoclinal upwarping of the Kenya-Uganda border area was accompanied by downflexing of the Turkana depression and local faulting⁷. A broad domal uplift of central Kenya of about 300 m in the late Miocene was succeeded by a major uplift of 1,400 m during late Pliocene to mid-Pleistocene times⁶. Fig. 2 shows isobases of the sub-Miocene erosion surface and indicates the sum of uplifts since the mid-Tertiary, which reached maxima of 1,700 m.

Rift Fault Pattern

The major faults define a complex graben (the Gregory rift⁸), which trends meridionally along the major axis of the uplift (Fig. 2). North and south of the Gregory rift, in Turkana and north Tanzania, the periclinal ends of the uplifted area are broad transverse depressions traversed by splay-faults. The major faults branching from the Gregory rift in these areas are antithetic in character and almost always down-throw eastwards.

The Gregory rift is in the central part of the Kenya rift zone, and is a complex graben 60–70 km wide bounded by major normal faults arranged *en echelon*. Broad step-fault platforms occur locally at each side of the graben, and between the hinge faults *en echelon* there are sloping ramps descending from the flanking plateau to the rift floor. The fault escarpments are well preserved and range up to 2,000 m in height in the central sector. The thickness of volcanics of the plateau (up to 2,000 m) and the still greater thickness of the volcanic and sedimentary fill in the rift floor which is inferred suggest that the throws of the major faults may reach 3,000–4,000 m. The floor of the Gregory graben, including the step-fault platforms and ramps, are cut by dense swarms of young, sub-parallel minor faults^{9–11}.

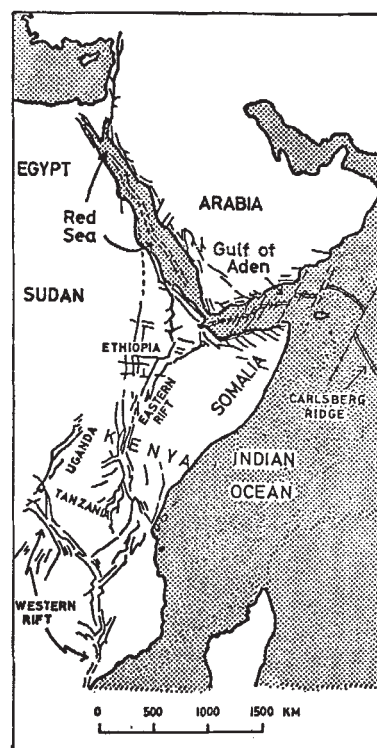


Fig. 1 Structural pattern of the Afro-Arabian rift system, showing the eastern and western rifts of Africa.

Notable features of the fault pattern are the element of symmetry about the minor (E-W) axis of the uplift and the location of the main rift on the crest and major axis. This bears out the view that there was a genetic connexion between epeirogenic upwarping and rift faulting.

Evolution of the Kenya Rift

The oldest recognizable rift structures are the dissected monoclinial flexure now represented by the Uganda escarpment⁷, and the related Turkwel fault (Fig. 3). They are mid-Tertiary, for they immediately pre-date the Miocene volcanics of the Turkana depression. An upwarped region along the Kenya-Uganda border was the site of lower to middle Miocene nephelinitic central volcanism¹², and the complementary Turkana depression was partly filled by contemporaneous flood basalts^{7,13}. In late Miocene times the central rift area was slightly uplifted, and was the site of massive fissure phonolite eruptions¹³.

The first extensive rift faults developed early in the Pliocene at the culmination of the Miocene uplift phase, producing a meridional asymmetrical trough faulted mainly on its western side (Fig. 4). There was relatively minor phonolite and trachyte volcanism in the floor of the central part of this trough in the mid-Pliocene, but this was followed by much more voluminous basalt eruptions along nearly the whole length of the trough together with the formation of the dominantly basaltic Aberdare central volcanic range¹³.

In late Pliocene times, massive eruptions of trachytic ignimbrites began in the Naivasha sector of the rift floor¹⁴, locally filling the rift and overflowing its flanks (Fig. 5). At about the same time, the last and major uplift of the marginal plateaux began, accompanied by the first of several phases of graben faulting, which created the outline of the Gregory rift. The developing graben was partly filled by lower to middle Pleistocene flood trachytes^{13,16}. Further local rejuvenations of the

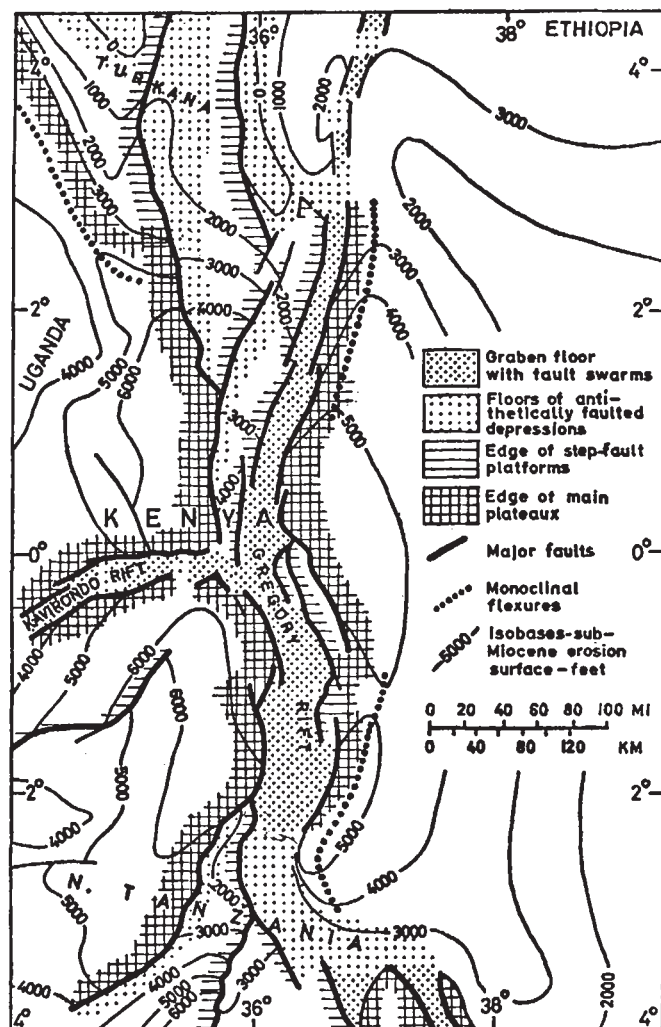


Fig. 2 Structure of the Kenya rift zone. The contours indicate the amount of crustal uplift since the mid-Tertiary in feet.

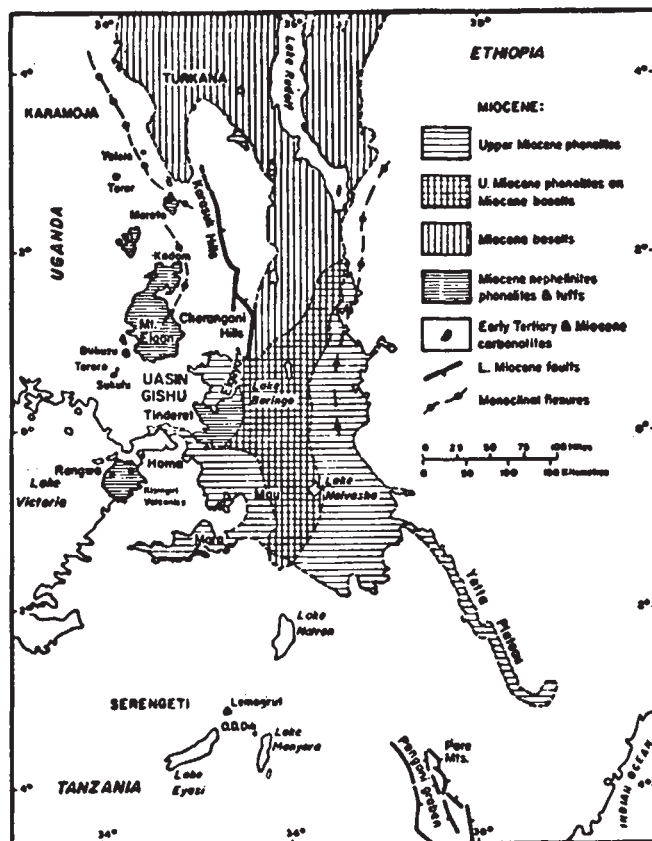


Fig. 3 Miocene volcanism and faulting in Kenya.

main graben and step faults continued until mid-Pleistocene times, deepening the Lake Naivasha and Lake Natron sectors. At the same time, the graben floor was shattered by swarms of closely spaced minor faults⁹⁻¹¹, which in some places reach densities of 2 to 3 faults per km (Fig. 6).

In the later Quaternary, trachyte, basalt-trachyte and phonolite caldera volcanoes¹⁵ built up axially in the floor of the inner graben, while in areas well to the east of the rift there were extensive basalt eruptions in three main areas forming linear multicentre volcanic chains¹⁶ (Fig. 6).

Thus in the Miocene, the Kenya rift passed through a period of broad crustal flexing and local faulting accompanied by basic volcanism, succeeded in the late Miocene by voluminous flood phonolite eruptions. The first faulting to affect the whole length of the rift took place in the early Pliocene, creating an asymmetrical graben. This was followed by dominantly basaltic volcanism in the floor of the rift depression, but towards the end of the Pliocene the last and major uplift of the plateaux began and was accompanied by massive trachytic volcanism and phases of graben faulting.

Kinematics of Rifting

The formation of the Gregory rift has been explained in a variety of ways—as a result of crustal doming¹⁷; of crustal stretching and thinning¹⁸; the subsidence of a block as a result of isostatic forces¹⁹; and as a zone of crustal rupture and injection of igneous rocks^{5,22}. The depth of the graben is too great for the doming or isostatic models to be adequate²⁰. If the fault planes have mean dips of 63°, there must have been at least 5 km of crustal extension to account for the observed structures. Since there are likely to be many concealed faults under the graben floor, the total crustal extension inferred on structural grounds could range up to 10 km, and this is much more than could result from crustal arching²¹, showing that the faulting cannot have been the result of doming alone,

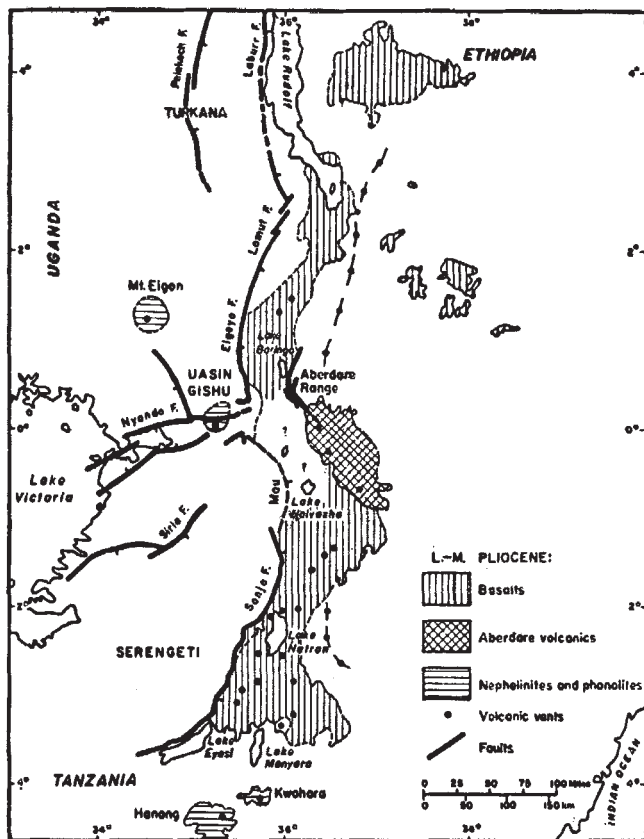


Fig. 4 Lower to middle Pliocene volcanism and faulting in Kenya.

so that both doming and faulting must be related results of some sub-crustal process.

In a model involving crustal disruption and separation^{5,24}, the maximum amount of crustal separation could not have been more than the 20–30 km width of the inner graben of the Gregory rift, for the step fault platforms bordering the inner graben locally expose Pre-Cambrian rocks and down-faulted formations of the adjacent plateaux. At the north and south extremities of the Kenya domal uplift, in southern Ethiopia and north Tanzania, Pre-Cambrian rocks outcrop across the whole width of the rift zone, showing that there can have been only about 3 km of crustal extension in those areas as a result of normal faulting. Thus the geological data will allow between 5 and 25 km of crustal extension (or separation) in the central sector of the Gregory rift but not more than about 3 km at its extremities. The absence of cross-rift faults of transform type that could account for large variations of crustal extension along the rift zone suggests that the crustal extension across the central rift was closer to 5 km than to 25 km.

There are sufficient gravity measurements²² in the area of the central Gregory rift to allow a Bouguer gravity anomaly profile to be drawn (Fig. 7a). The usual specific gravity of 2.67 has been used for the Bouguer reduction to sea level, with the result that the structural complexity and the existence of some thousands of metres of low density volcanics on the flanks and in the floor of the rift exert a strong influence on the shape of the profile. In a computed²³ two-dimensional model of crustal structure (Fig. 7b) we have included low density zones (specific gravities 2.0 and 2.2) on each side of the rift valley to minimize the insufficient Bouguer compensation resulting from the presence of these low density volcanics. The computed Bouguer anomaly of the model agrees with the observed profile within reasonable limits (Fig. 7a). To explain the positive peak in the profile, the model has to contain

an intra-crustal body with a positive specific gravity contrast of 0.15, the top of which is 10 km wide and reaches through the crust to 1,500 m below sea level under the inner graben of the Gregory rift. This body (specific gravity 3.05) could represent a wedge shaped basic intrusive mass. Other interpretations of the gravity data yield similar crustal models^{22,24}, but with wider (16–28 km) dense bodies beneath the rift floor.

Support for the presence of a zone of low density upper mantle beneath the rift comes from interpretations of Bouguer gravity anomaly profiles across the East African plateau^{18,25} and from observation of P wave delays (personal communication from E. B. Rodrigues), S wave attenuation²⁶ and studies of seismic wave transfer spectra²⁷ for paths along the rift to the Nairobi WWSS station by comparison with paths of other azimuth. The presence of a relatively high density body within the crust beneath the rift valley is also suggested by preliminary results of seismic refraction work, which indicates the presence of a body with a seismic velocity of 6.5 km/s less than 20 km beneath the north-central part of the Kenya rift²⁸. Similar conclusions have been drawn from earthquake studies of the western rift²⁹.

The crustal model (Fig. 7b) suggests there has been about 10 km of crustal separation under the central part of the Gregory graben, together with the injection of basic igneous rocks derived from a presumably hot and partly molten zone of low density in the upper mantle. The centre of the basic intrusive body on the profile lies just south of Menengai crater (Fig. 6), and the gravity measurements show that it trends NNW and SSE along the floor of the inner graben. The rift floor in the zone above the basic intrusive body consists of late Pliocene ignimbrites overlain by lower Pleistocene trachyte lavas, and there is nothing to distinguish its structure from the rest of the rift floor, nor is it characterized by any alignment of volcanic centres¹⁰. There are no quater-

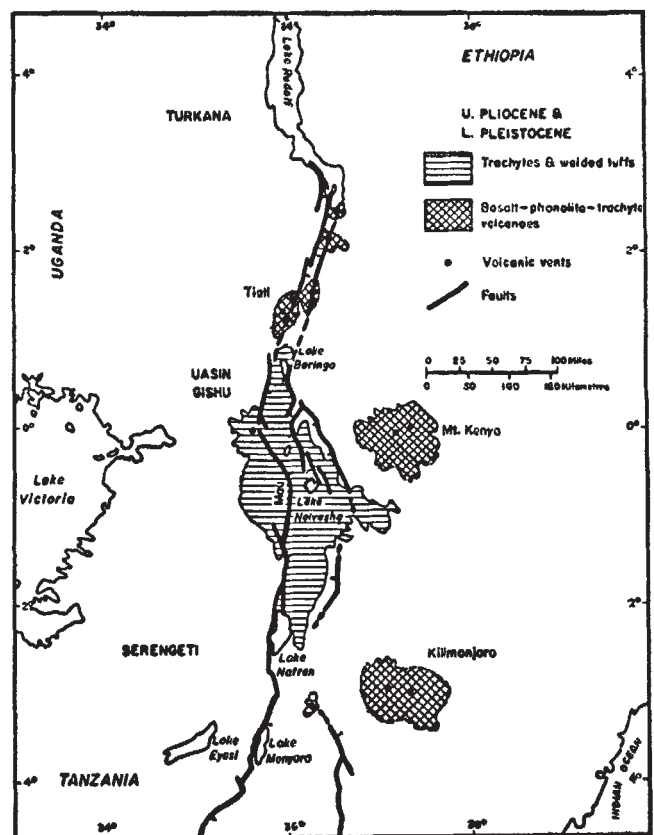


Fig. 5 Upper Pliocene and lower Pleistocene volcanism and faulting in Kenya.

nary basalt volcanoes in this area, and they are extremely rare throughout the Gregory rift¹⁶.

Since it is most probable that basic igneous injection into and through the crust would be accompanied by basaltic volcanism and structural effects, it is probable that the period of crustal separation and basic igneous injection took place in pre-upper Pliocene times, perhaps at the time of the extensive mid-Pliocene basalt eruptions that flooded much of the rift floor (Fig. 4) or during the Miocene basaltic volcanism (Fig. 3). The massive late Pliocene and Quaternary sialic volcanism of the central Gregory rift, which produced about 100,000 km³ of trachytic eruptives¹⁶, evidently succeeded the period of crustal separation and concealed its volcanic and tectonic effects. What kind of petrogenetic process produced this large volume of trachytic eruptives is uncertain³⁰, but it is possible that crustal disruption and basic igneous injection was followed by anatexis of fenitized sialic rocks¹² or by some form of crustal assimilation³¹.

The 10 km of crustal separation beneath the central Kenya rift suggested by the gravity data is much less than the 30 km of crustal separation suggested by plate tectonics⁵. Recent modifications^{32,33} to the plate tectonics scheme, which involve bringing the Arabia-Nubia and Arabia-Somalia rotation

and ended with regional uplifts and intermediate and silicic volcanism, during and after which the main graben faulting occurred. The later and most important of these episodes was accompanied by the eruption of such large volumes of trachytic ignimbrites that it is reasonable to suppose that part at least of the collapse of the floor of the Gregory rift resulted from the rapid eruption of lava. The surface geology of the floor of the central Kenya rift does not show features related to 10 km of crustal separation, but since the pre-Quaternary structural history of the inner graben is largely conjectural, this means that the crustal separation must have taken place mostly in the Tertiary, its effects being subsequently obscured by later volcanics and sediments which partly filled the graben.

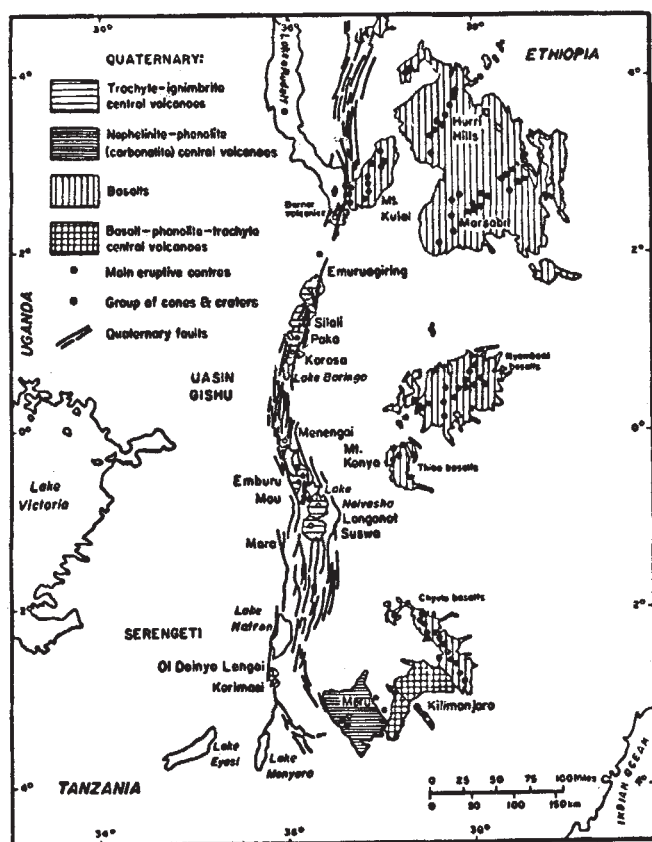


Fig. 6 Late Quaternary volcanism and faulting in Kenya.

poles closer together, does, however, imply a much reduced crustal extension across the eastern rift, closer to the 10 km indicated by the gravity data.

In summary, it seems that the formation of the Kenya rift valley is the result of phases of epeirogenic uplift, volcanism and faulting since lower Miocene times. The underlying process seems to have been the rise of geotherms in the upper mantle, leading to partial melting and regional up-doming of the crust. The main Miocene and late Pliocene-early Pleistocene taphrogenic episodes began with basic volcanism accompanied by crustal disruption and magmatic injection,

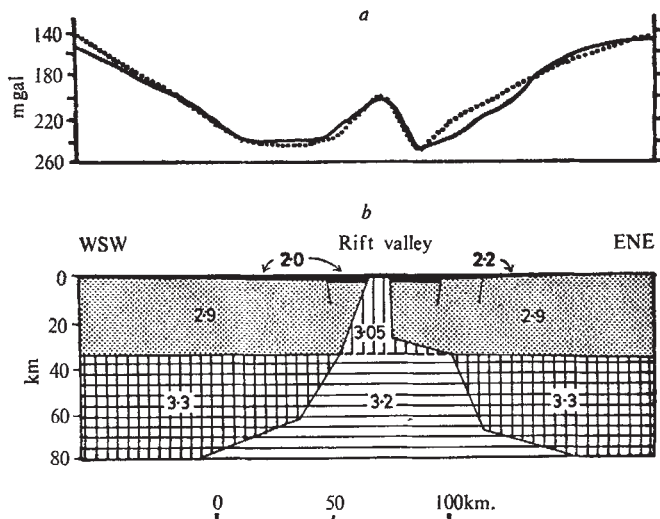


Fig. 7 a, Bouguer gravity profile across the Gregory rift, orientated ENE-WSW, and crossing the central rift just south of Menengai (see Fig. 6). The continuous line is the observed Bouguer gravity anomaly and the dotted line is the computed anomaly for the crustal model shown in b.

Although the Kenya rift is linked to the world rift system, and the underlying mantle processes are probably similar throughout the system³⁴, it should not be regarded as a model for oceanic ridge-rifts nor even as a typical example of the first stage of continental break-up. The mean spreading rate of the Kenya rift is not more than 0.5 mm a year compared with 1-2 cm a year of the Red Sea and Gulf of Aden and 2-10 cm a year for the mature mid-ocean ridges³⁵. Hence the Kenya rift is best regarded as part of a weak branch of the Carlsbad-Sheba ridge-Red Sea axial trough spreading axis, characterized by exceedingly slow rates of crustal extension and by long-continued interaction between crust and thermally activated mantle.

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Parameter Sensitivity as a Criterion for Evaluating and Comparing the Performance of Biochemical Systems

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Parameter sensitivity is a theoretical criterion that can be used in the quantitative evaluation and comparison of different biochemical systems that regulate, for example, the supply of end product.

REPRESSION of enzyme synthesis and inhibition of enzyme activity by the end product of a biosynthetic sequence, sometimes operating in conjunction, serve to regulate the supply of the end product¹. The energy conserved in these ways by producing only the necessary complement of enzymes and intermediate metabolites is also believed to be a significant contribution to the efficiency of the organism. Although these ideas have been apparent since the initial discoveries in this area, there have been few attempts to establish criteria by which the effectiveness of different systems in performing these functions can be evaluated and compared. This seems to be true for biochemical systems in general. Although there are numerous physical and chemical techniques for characterizing the components of a biochemical system, there are relatively few quantitative measures for those specific properties and behaviour patterns, such as regulation, that emerge at the level of organized networks of enzyme-catalysed reactions.

One quantitative measure for the performance of a regulated biosynthetic pathway is provided by the relative growth rates of two strains of bacteria that are presumed to be identical, except for a difference in the control of a pathway. This criterion has been useful in investigating the evolutionary advantage conferred on an organism by biosynthetic pathways controlled by repression² or by end product inhibition³.

This measurement actually determines "selective advantage" and as such it is a complex mixture of effects related to both the organism and its environment. Indeed, as these studies have shown^{1,2}, the ratio of the growth rates of the two organisms is strongly dependent on the type of medium used to support their growth. From this we conclude that the rate of growth is related only in a rather non-specific way to the function of the particular control system under consideration. Furthermore, unless special precautions are taken to ensure that the pathway in question is rate-limiting for growth, this measurement may actually reflect secondary changes in the total metabolism of the cell rather than changes in the primary function of the modified control system. These ambiguities indicate that a more specific criterion of performance is needed for such biochemical systems.

Ideally, we should like criteria for measuring the effectiveness of a biochemical control system to meet the following requirements. First, they should be quantitative. This is for greater objectivity and for distinguishing not only a completely functional from a completely nonfunctional system, but a spectrum of systems functioning with different efficiencies. Second, they should be relevant. By this I mean the criteria must be directly related to the particular function of the system in question, thus avoiding confusion with irrelevant or secondary phenomena. Finally, they should be invariant. They should represent an intrinsic property of the system that relates changes in the system or its environment to the resulting changes in the behaviour or response of the system; and such relationships should be unaffected by the particular magnitude of the change or the particular way in which the original change was produced.

To facilitate the remaining discussion I shall consider the didactic system shown schematically in Fig. 1; it may be thought of as a biosynthetic pathway consisting of a single enzyme subject to repression at the transcription level with the end product as the co-repressor. One of the primary

functions of such a control system is presumably to maintain a relatively constant supply of the end product in spite of changes in the system itself or in its environment. In this communication the criterion of parameter sensitivity is defined as relevant for assessing the ability of such control systems to "buffer" the end product concentration against changes internal to the system itself. This aspect of biochemical feedback control is just as important but less often appreciated than its ability to counteract changes in the environment. An analysis of the effects of environmental changes is presented elsewhere (my unpublished work).

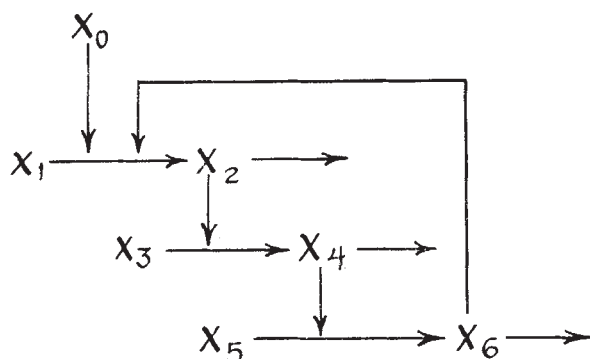


Fig. 1 A schematic representation of a biosynthetic pathway consisting of a single enzyme whose synthesis is subject to repression at the transcription level and whose end product serves as the co-repressor. X_0 , Structural gene for the enzyme; X_1 , weighted sum of the nucleotide pools; X_2 , specific messenger-RNA; X_3 , weighted sum of the amino-acid pools; X_4 , enzyme; X_5 , substrate; and X_6 , end product. The transfer of material from one pool to another is represented by an arrow from the symbol denoting the original pool to the symbol denoting the final pool (for simplicity the explicit representation of the final pool is in some instances omitted). A modification of this transfer by a third substance is represented by an arrow from the symbol denoting the modifier to the middle of the arrow representing the transfer. All the modifications in this diagram are positive except for the modification of the $X_1 \rightarrow X_2$ reaction by X_6 , which is negative since X_6 acts in conjunction with other molecules to repress this conversion. Those additional modifiers and/or "cofactors" that are not of primary concern here have been omitted from the diagram.

The following definition of parameter sensitivity meets these requirements and avoids the difficulties encountered in measuring the effectiveness of a biochemical control system that I have mentioned. If a parameter is a property of the system that is normally a fixed quantity, and is in different systems or in different environments, parameters can assume different values—for example, in a simple enzyme catalysed reaction, the Michaelis constant K_m would be a parameter of the system, whereas the concentration of the substrate would be a variable—in the steady state, the relative variation (or percentage change) in some property X , related to the system function in question, with respect to the relative variation of a parameter α , is defined as the parameter sensitivity of X with respect to α , that is,

$$S_{\alpha X} = \frac{\delta X}{\delta \alpha} \frac{\alpha}{X} \quad (1)$$

This is a general definition and can therefore be applied to many different functions and parameters in a wide variety of systems. In experimental practice, the parameter sensitivity would be measured using finite differences, and the expression in (1) would be approximated as

$$S_{\alpha X} = \frac{X_2 - X_1}{X_1} \frac{\alpha_1}{\alpha_2 - \alpha_1} \quad (2)$$

where the subscripts 1 and 2 refer to values before and after a change in the parameter value respectively. In reference to

Fig. 1, we shall consider the concentration of the end product as a property directly related to the function of the system, as this function is described in the previous paragraph; the molecular activity or turn-over number of the enzyme is considered an intrinsic or characteristic parameter of the system. Thus the parameter sensitivity of the end product concentration, X_6 , will be examined in response to changes in the molecular activity of the enzyme, α .

One might imagine this change in molecular activity to be produced in any of a number of ways. We shall assume that a mutation in that portion of the genome coding for the biosynthetic enzyme has caused a partial loss of activity in the enzyme molecules. Other things being equal, the effect of such a change would be a reduction in the concentration of the end product, and consequently in the rate at which it is used up, until the rate of utilization balanced the new, reduced rate of synthesis. This reduction in the concentration of the end product, however, would tend to derepress the synthesis of new enzyme molecules, which in turn would increase the rate of synthesis of the end product back toward its normal level. Thus, the activity of the enzymes present is decreased, but the quantity of the enzyme is increased by derepression. The net effect is but a slight decrease in the supply of the end product. These qualitative results are fairly self-evident. The important point for this discussion is that the more effective the compensation by derepression, the smaller the resulting change in the concentration of the end product for a given change in the molecular activity and, therefore, the lower the parameter sensitivity. Thus, parameter sensitivity in this example measures the effectiveness of feedback repression in compensating for internal changes.

A numerical value for the parameter sensitivity in this case could be obtained by measuring the molecular activity of the mutant and wild type enzymes, as well as the endogenous concentration of the end product in steady state for both the mutant and wild type organism. Although we are not primarily concerned here with details of the experimental measurements, it could be pointed out that it might be difficult to determine the conditions in which the molecular activity should be measured *in vitro* so as to mimic the value existing in the cell. One might hope, however, that these values would differ by the same percentage for both the mutant and the wild type enzyme. If this were so, then the calculation of percentage variation due to mutation would be unaffected by the changes in each of the individual measurements. A more detailed analysis of parameter sensitivity shows that alternatively one may utilize the expression $-(\delta X_6 / \delta X_4)(X_4 / X_6)$ as a close approximation to the true value when the parameter sensitivity is slight. In this method one would measure differences in the amount of wild type and mutant enzyme rather than differences in their molecular activity. Changes in the concentration of the end product could be measured by a number of chemical, enzymatic, or radioisotopic techniques.

Suppose that in the mutant organism there is a 10% decrease in molecular activity and a 1% decrease in the end product concentration; this parameter sensitivity of the control system would have a value of 0.10. This number is a constant independent of the magnitudes of the changes over some appropriate range and it is therefore characteristic of the particular system under consideration. The consistency of this relation is due in part to the fact that one is dealing with a ratio of changes. Thus, one would get the same result if a 20% decrease in molecular activity were to cause a 2% decrease in the end product concentration. Furthermore, the use of percentage variation tends to eliminate the differences in absolute magnitude that might be produced by different environmental conditions. The constancy of this relation also makes it useful for predictive purposes. Once this parameter sensitivity of the system has been determined with one type of mutation, one can calculate from observed changes in the end product concentration what the changes in molecular activity must be for a different mutation in the same cistron. Con-

versely, from a knowledge of the changes in molecular activity, one can predict what the changes in the end product concentration will be.

It should be emphasized that this important property of the intact system can in no way be obtained solely from experiments with the individual components or reactions of the system. Biochemical feedback regulation and the parameter sensitivities in such systems are properties that emerge only at the level of integrated networks of reactions. As more detailed analysis shows (my unpublished work), however, parameter sensitivity can be determined from a knowledge of the individual components of the system when this knowledge is coupled with an appropriate method of systems analysis or, alternatively, from direct physiological measurements in the intact system, as I have indicated.

The effect of change in other parameters could be investigated, and the mechanism for introducing a change in parameter value need not be genetic mutation. One could also

examine other properties of the system besides the supply of the end product, but the choice in each instance will be guided by the hypothesis concerning the function of the system. The concept of parameter sensitivity is not restricted in any way to the example used here for illustration. For example, this concept has been used successfully in a comparative analysis of biosynthetic pathways subject to feedback control by inhibition at the molecular level (my unpublished work). Thus the criterion of sensitivity provides a useful quantitative tool for evaluating and comparing the effectiveness of biochemical systems.

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Variability of X-ray Emission from M87

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New rocket observations of this galaxy, distinguished by an optical jet 1,500 parsec long, suggest a variable X-ray emission probably linked with inhomogeneities in the jet.

We first reported¹ X-ray emission from the direction of M87 in 1965 (ref. 1) and several measurements²⁻⁴ have subsequently been made. The position of the X-ray source has been fixed in declination to ± 0.1 degree by a fan beam scan. The new observation reported in this article places the source inside an error box of 0.1 square degrees that includes M87. Both the flux and the shape of the X-ray spectrum in the present observation differ markedly from previous observations, implying a high degree of variability. Evidence for X-ray emission from the quasar 3C 273 was also obtained, although with much lower statistical significance than for M87.

Observation of M87

On March 28, 1969, observations were carried out with two proportional counters aboard an Aerobee-Hi rocket which was launched from White Sands Missile Range. Each counter was equipped with a multiple slit collimator exposing a field of view of $1^\circ \times 8^\circ$. The slit orientations were crossed as shown in Fig. 1. The window material was 0.00015 inch "Mylar" coated with 70 Å of evaporated nichrome and the gas filling was a mixture of 90% argon and 10% methane at a pressure of 16 pounds per square inch. The unobscured window area of each counter was 254 square centimetres. A plastic anti-coincidence shield surrounded each counter on five sides. All of the available observing time was devoted to a slow scan across 3C 273 and M87 as shown in Fig. 1 and the direction of pointing was determined from star field photographs taken every 5 s.

To produce the scanned data plotted in Figs. 2 and 3 the individual count versus time were matched at the instant of crossing of each source and the counts from both counters were summed. M87 was clearly detected with large signal-to-noise ratio by each counter; 3C 273 produced a signal equivalent to three standard deviations (3σ) only in the summed scans of both counters. By means of pulse height analysis, the spectrum of M87 was derived as shown in Fig. 4. A similar observation by Adams *et al.* nine months earlier indicated a much harder spectrum and a flux in the 1–10 keV range roughly an order of magnitude greater. There is no evidence of self absorption in the source. Table 1 lists all the observations reported for M87 up to the time of the last NRL flight, and it is clear that the range of flux values seems to be several times as great as any possible systematic errors in the individual measurements.

Table 1 Observations of X-rays from M87

Observer	Flux (erg cm ⁻² s ⁻¹)	Energy range (keV)
NRL (1965) ¹	$(2 \pm 1) \times 10^{-9}$	1–10
NRL (1967) ²	$(8.7 \pm 2) \times 10^{-10}$	1–10
MIT (1967) ³	$(5 \pm 2) \times 10^{-10}$	1.5–6
Leicester (1968) ⁴	$(1.5 \pm 0.3) \times 10^{-9}$	1.5–5
NRL (1969)	$(1.9 \pm 0.2) \times 10^{-10}$	0.8–4

A number of balloon flights have been made in attempts to observe M87 at energies above 25 keV. Haymes *et al.* claimed⁵ a significant result in 1967 at about 40 keV, which falls on the extrapolation of the radio spectrum with a single power law index of -0.7 extending all the way from radio through optical to the X-ray wavelengths. Two attempts by the UCSD group⁶ in February 1967 and in June 1968 did not, however, detect the source and gave upper limits significantly below that claimed by Haymes *et al.* Overbeck and Tannenbaum⁷ in 1968 and McClintock *et al.*⁸ in 1969 estab-

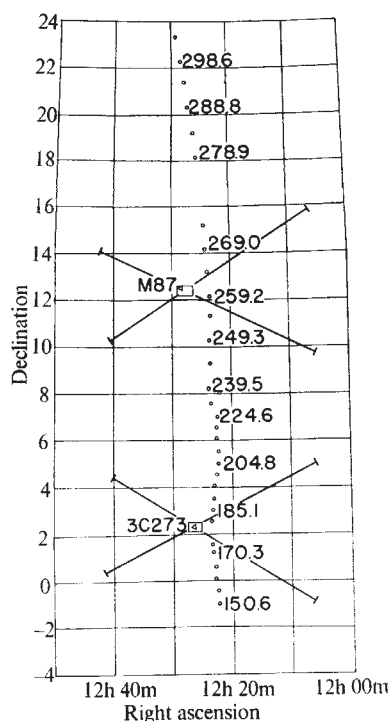


Fig. 1 Scan track across 3C 273 and M87. Each counter was equipped with a $1^\circ \times 8^\circ$ collimator. The collimators were crossed as shown by the bars representing the 8° dimension. Open circles identify positions of the centre of the field of view at the indicated times in seconds from launch. Triangles give the positions of 3C 273 and M87 within error boxes of the measurements.

lished 2σ upper limits which are less than the flux claimed by the Rice University group, but a Rice University balloon observation in 1968 (ref. 9) produced essentially the same result as in the 1967 flight. It remains uncertain, therefore, on the basis of all of these balloon observations whether the spectrum does in fact extend to $E > 25$ keV without an increase in spectral index or whether the flux is variable.

The Virgo Cluster

M87 lies in the midst of the Virgo cluster which contains some 2,500 galaxies within a field of about 12 degrees diameter. About 80 per cent of the cluster was scanned by the detectors in our March 1969 flight, during the time interval 230 s to 280 s. The lower graph of Fig. 2 shows how the number of galaxies in the field of view varied with time. The signal from M87 stands above a general increase in background which may be associated with the large number of normal galaxies in the cluster. If we average the background from 230 s to 280 s, excluding the interval that contains M87, we obtain 17.3 counts per second which is about 7σ above the average of 13.7 counts per second for the background in the 280 s to 320 s interval outside the cluster. The increment of background flux amounts to 8×10^{39} erg s^{-1} per galaxy (1–10 keV) if the average distance is taken to be that of M87, 14.8 megaparsec, and the average spectrum is assumed to be a power law of index -1 . In an analysis of the distribution of X-ray sources within our galaxy, we had estimated¹⁰ a total X-ray luminosity for the galaxy of 7×10^{39} erg s^{-1} which is in close agreement with the figure we now obtain for the luminosity per galaxy from an average of 2,000 galaxies in Virgo.

Observation of 3C 273

In 1967 a scan was made of the position of the quasar 3C 273. There was some evidence² of X-ray flux at a level of

about 2×10^{-10} erg cm^{-2} s^{-1} (1–10 keV) but the statistical measure of the signal did not exceed two standard deviations (2σ). If taken as an upper limit, the measurement implied that the X-ray power did not exceed 7×10^{45} erg s^{-1} . A simple extrapolation of the -0.7 radio-optical spectral index to the X-ray range would predict a flux of about five times the upper limit of the 1967 observation.

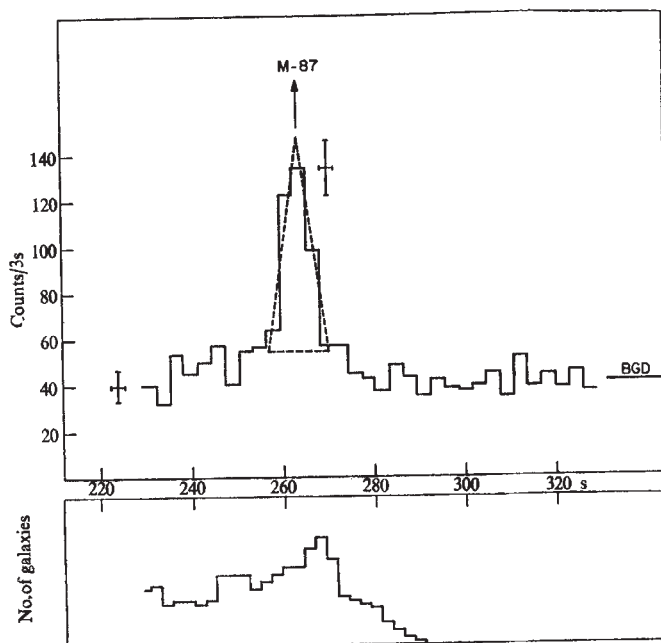


Fig. 2 Scan across M87. Signals from both counters were matched at their peaks and summed over the range shown above. The relative number of Virgo Cluster galaxies in the field of view of both counters is plotted below. BGD is the background level obtained by excluding the M87 signal and averaging the entire count from -2° to $+22^\circ$ declination.

A scan of 3C 273 was included in the March 1969 NRL flight with the results shown in Fig. 3. If background is taken to be the average over the entire 20 degree scan track from -2 degrees to $+24$ degrees declination (with the M87 counts removed), the peak signal at the position of 3C 273 stands 3σ above background. The spectral range was 1 to 4.5 keV and the flux was 6×10^{-11} erg cm^{-2} s^{-1} , about one-fifth of the flux from M87. The corresponding X-ray power is about 2×10^{45} erg s^{-1} for a distance of 500 megaparsecs.

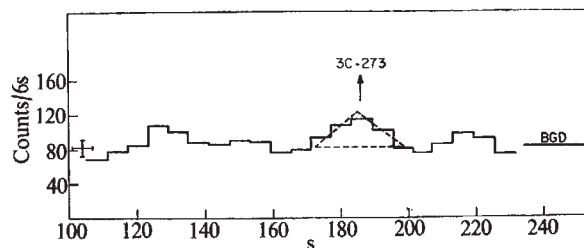


Fig. 3 Scan across 3C 273. Signals from both counters were matched at sec and summed over the range shown above. The controlled scan began at 150 s. Manoeuvres between 100 and 150 s included a large area of sky outside Virgo.

Bowyer *et al.* observed 3C 273 on June 14, 1969, and reported¹¹ a flux of 3×10^{-10} erg cm^{-2} s^{-1} (1–10 keV), which is several times greater than the flux which we observed less than three months earlier. It may be premature, however,

to conclude that such high variability is characteristic of 3C 273, considering the marginal nature of the detections.

Discussion

In the radio spectrum, M87 is characterized as a core halo source (Virgo A). An extended optical jet emerges from the nucleus to a distance of at least 1,500 parsecs. The light of the jet is strongly polarized and the radiation mechanism is undoubtedly synchrotron. Recent refinements in both optical¹² and radio resolution¹³ have revealed that the jet is composed of several optically bright knots, no more than a second of arc in diameter, and that the radio core contains a compact source with a diameter of 2.5 light months and a luminosity of 10^{39} erg s⁻¹ in a band of 10^{10} cycles about a frequency of 0.23×10^{-10} Hz.

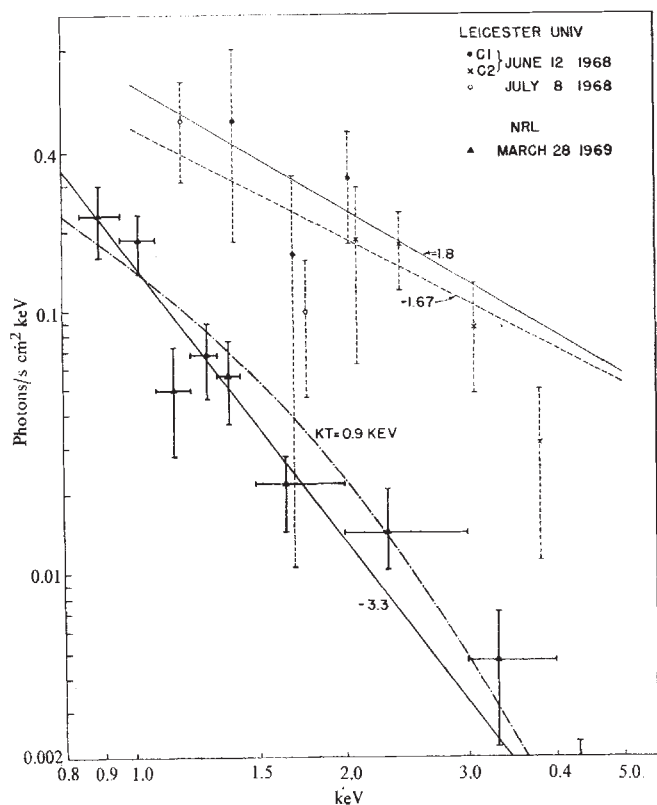


Fig. 4 Spectra of M87 obtained from two flights by the Leicester University group and the NRL flight described here. The photon power law indices are indicated on each curve. Also shown is a possible bremsstrahlung fit to the NRL data with $kT=0.9$ keV.

When the earliest X-ray results at 1 to 10 keV were fitted to a single power law spectrum with index -0.7 extending all the way from radio through optical to X-ray wavelengths, this remarkable fit over more than nine decades of frequency suggested the possibility that synchrotron radiation generated by relativistic electrons emerging from the core and traversing the jet was responsible for the entire spectrum¹⁴. The lifetime of the electrons would, however, be too short to cover the distance from the core to the end of the jet even for the optical radiation—for an equipartition field of about 3×10^{-4} gauss, the optical lifetime is about 100 years. To avoid the problems of electron lifetime it was proposed¹⁵ that relativistic protons are initially injected and interact with the ambient gas of the condensations in the jet to produce pions. The pions subsequently follow the π - μ - e decay sequence to yield relativistic electrons. Felten¹⁶ has argued that this model suffers from

difficulties in explaining the absence of gamma ray emission from π_0 decays. The predicted gamma photon flux of 4×10^{-10} cm⁻² s⁻¹ is well above the observational upper limit of about 5×10^{-11} cm⁻² s⁻¹. He also pointed to the difficulty of accounting for enough ambient gas to balance the cosmic ray pressure in the condensations.

The evidence for variability in Table 1 and Fig. 4 lends support to models which associate the emission with the recently revealed compact sources in the nucleus and the jet. According to Burbidge¹⁷, the energy density of radio photons and the energy content of relativistic electrons in the compact nuclear core may be sufficient to provide the observed X-ray emission by Compton scattering. Several years ago, Shklovsky¹⁴ noted that the X-ray power of M87 is about three orders of magnitude greater than the luminosity in optical line emission from the core of the galaxy. If the X-ray source were concentrated in the nucleus, it would be enveloped by cold plasma which it would ionize and excite to line emission. The relative weakness of the line emission must therefore imply that only a very small part of the X-ray emission, if it originates in the core, is absorbed. Shklovsky therefore suggested the possibility that the core plasma was concentrated in several condensed bodies distributed with sufficient inhomogeneity so that only about one per cent of the core volume (radius 30 parsec) is obscured by these dense bodies.

Burbidge has also proposed that the knots on the jet may be clusters of massive compact objects, surrounded by magnetospheres, which are expelled from the nucleus. If these are pulsar-like stars, as many as 10^6 to 10^7 per optical knot would be required. Shklovsky¹⁸ refers to large rotating magnetized plasma bodies as "magnetoids" and suggests that each condensation in the jet of M87 is a small magnetoid ($10^4 M_\odot$) similar to a quasar. The light radiated by the magnetoid should be variable in flux and polarization.

More accurate and complete information on this variability would provide important clues to the sizes of the radiating regions. Such data may be forthcoming from the recently launched X-ray astronomy satellite SAS-1 of NASA. The size of the jet in M87 is large enough (20 arc s) so that it is even within the realm of present day rocket astronomy to discriminate between emission from objects in the jet or from the nucleus.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Probability of Long Period Gravitational Radiation

BECAUSE there has been no published support yet for Weber's detection of gravitational waves¹, I venture to report an experiment at its early stages.

While several researchers have considered searching for gravitational radiation or supposedly related events² at relatively high frequencies, I considered looking in the low frequency range near and below 1 Hz. This is made possible through the method used in deep space probe tracking³, which in recent years has obtained an accuracy of 1 part in 10^{12} . Basically, my experiment consisted of searching for variations in the expected Doppler frequency of signals returning to Earth from Mariner 6 or 7, while the spacecraft were at distances from the Earth comparable with the wavelength of such long period gravitational radiation that might exist.

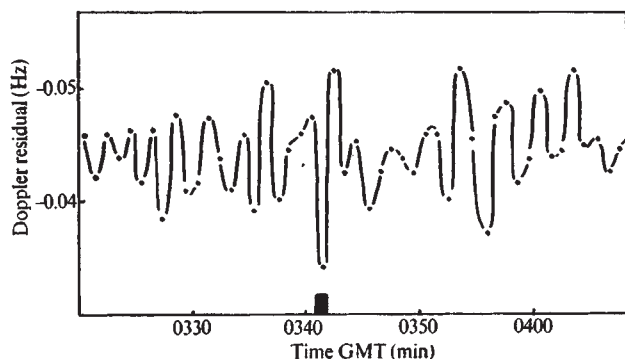


Fig. 1 Actual Doppler residuals remaining after taking out the correction for the spacecraft's calculated trajectory. The interval of significance (0341) is indicated by a black bar. These data are for Mariner 6 on March 15, 1969.

Unlike Kaufmann⁴, my proposal was not concerned with the detection of the gravitational Doppler effects on the electromagnetic radiation. These are several orders of magnitude below the sensitivity of the present equipment. Rather I was concerned with detection of the direct effects of gravitational radiation on the spacecraft's trajectory.

For this experiment I was limited to sampling rate intervals of 60 s. I considered the difference in the dispersion factor between the frequencies of Weber (10^3 Hz) and those available to me for analysis (10^{-2} Hz) to be small, and so I considered near simultaneous events.

There were four records of Doppler data available, covering times of particular events indicated by Weber in his first report⁵. Because of a high background noise level, two of these were unusable. Of the others, the first indicated that something had occurred at the upper frequency limit of the data (0.0083 Hz). This event is seen in Figs. 1 and 2. Noise factors include variation of electron density along the path of propagation, ionospheric changes, instrumental stability, and

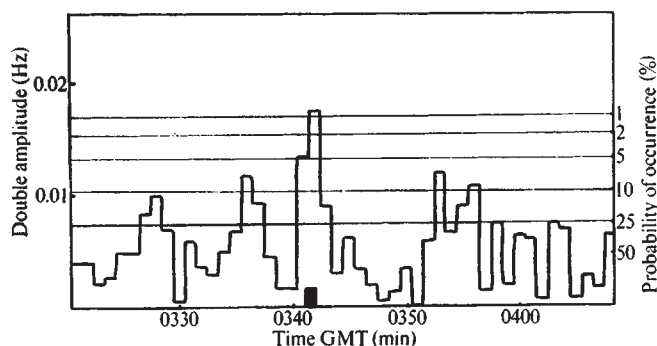


Fig. 2 The double amplitude 2 min period noise (0.0083 Hz). The probability of occurrence for such amplitudes for this day is given in per cent. The probability for the amplitude at 0341 is 0.7%.

long period gravitational radiation. Clearly something unusual happened around the interval of Weber's event at 0341 GMT on March 15, 1969.

Such gravitational waves as the one I have indicated cause a maximum velocity change of the spacecraft of less than 3 mm s^{-1} as seen from Earth. This, if integrated over an interval of 60 s, indicates a displacement of the body by ~ 10 cm over a total distance of measure between the Earth and spacecraft of approximately 10^{12} cm, a displacement of 1 part in 10^{11} . Weber measured 1 part displacement in 10^{15} at a higher frequency, using only a fraction of the wavelength. During a time interval 10^5 larger than Weber's I observed a relative displacement 10^4 larger. The form of the Doppler pattern indicates that the disturbance caused a dilatation at onset across the detector system. This is what was expected from a gravitational wave, unlike some other noise sources. On the other record, 0312 GMT, March 21, 1969, I observed longer period disturbances (10^{-3} Hz) indicating similar velocity changes and a similar Doppler pattern. Generally one should expect greater velocity changes between 10^{-2} Hz and 1 Hz. This region will be investigated later, when I can obtain sampling rate intervals of 1 s, not available for normal tracking purposes. Smaller sampling rate intervals contain more noise, but it is not expected that the amplitude

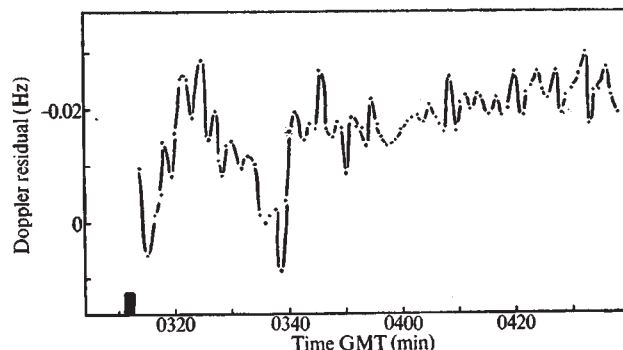


Fig. 3 Actual Doppler residuals following the event of 0312 GMT, March 21, 1969. This is plotted 1/2 scale to the previous event. Such large disturbances rarely occur.

of this noise will generally increase as rapidly as the amplitude of the gravitation radiation; more coherent patterns can be established.

According to Weber's most recent results⁶ the most probable direction of these waves is aligned with the direction of the galaxy centre. Using this method the response is therefore directly a function of $\cos \alpha$, where α is the angle between the line of sight to the spacecraft and the direction of the galaxy centre. It is hoped that with refinements in analysis, shorter sampling rates, and wavelength and angle determinations, future correlations can be improved considerably. Indeed, with the present sampling rate, I did not expect a favourable result.

I thank Jack Lorell of the Tracking and Orbit Determination Section of the Jet Propulsion Laboratory in Pasadena for Doppler tracking data, and Joe Weber, who inspired these observations.

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Abundances and Acceleration Mechanisms of Cosmic Rays

MEASUREMENTS of the chemical composition of cosmic rays¹ have shown that for most elements the abundances roughly correspond to their universal abundances. I wish to point out here that some systematic differences occur in the low energy range, which are correlated with the first ionization potentials of the corresponding elements.

In Fig. 1 I have plotted the ratio of the cosmic ray abundance¹ to the "normal" stellar abundance² for the different elements. The results are given for cosmic ray abundances in three different intervals. The elements Li, Be, B and F are omitted from the figure. The large overabundances of Li, Be and B are probably due to spallation. The element F is undetected in several energy ranges, but may be overabundant in the 50–200 MeV/nucleon range. The uncertainties in the cosmic ray abundance and "normal" star abundance are, however, large.

It is apparent from Fig. 1 that there is a significant correlation between first ionization potential and relative abundances of the cosmic rays in the lowest energy range. The relative abundances range from an overabundance of the order of 10 for elements with the lowest first ionization potentials to underabundances of the order of 10 for elements with the highest first ionization potentials. In the energy range 200–5,000 MeV/nucleon the same correlation may also be present while the picture seems to be more complicated for the highest energy range. In this energy range the correlation is possibly present for the lighter elements up to Ca. On the other hand, for the elements from Sc through the iron group and up to Ni there is no systematic behaviour in terms of the first ionization potential. These elements have approximately equal first ionization potentials but their relative cosmic ray abundances range from an overabundance of more than 1,000 in the case of Sc to a nearly normal abundance for Fe.

The observed correlation at the lower energies suggests strongly that low energy cosmic rays have initially been

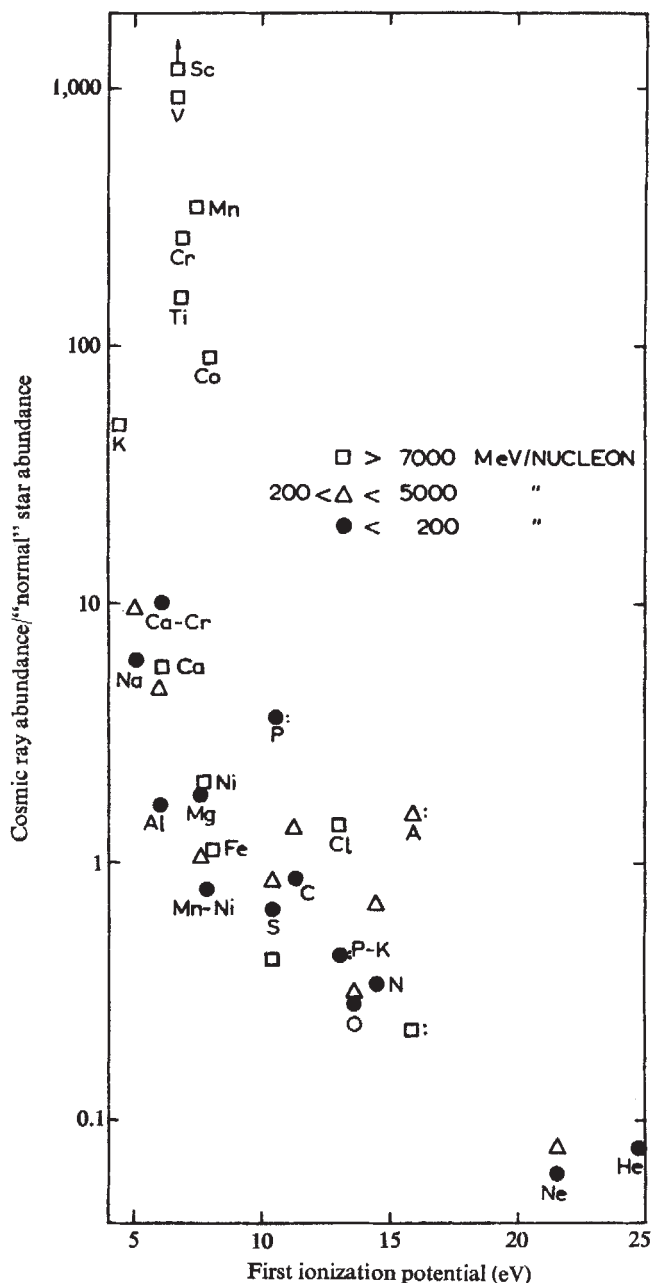


Fig. 1 The ratio of the cosmic ray abundance for the different elements at three energy intervals to the "normal" star abundance against the first ionization potential of the corresponding elements. For the "normal" star abundance, I used an average of the results given by Unsöld² with the exception of the abundance for A which was taken from the work of Pottasch⁴ and the solar abundance for Fe which was taken from the work of Garz *et al.*⁵.

accelerated in a process where electromagnetic forces have acted on a gas of normal composition that is partly ionized as a consequence of normal thermal or radiative processes. In such a gas the elements with low first ionization potentials are preferentially ionized and may therefore be accelerated by the electromagnetic forces. But the elements with high first ionization potentials are less likely to be ionized and will therefore have a smaller probability of being accelerated. I do not expect a violent event, in which the overall ionization state is high, to give rise to the observed cosmic ray abundance spectrum at low energies. Such violent events may be a more likely explanation for the cosmic rays at higher energies.

The findings reported here apparently require more than one type of cosmic ray source. This is in accordance with the conclusions reached by Comstock³ on the basis of the shape of the energy spectrum at low energies.

Possible regions of partly ionized matter accelerated by electromagnetic forces are (i) shells of supernovae, in which the accelerating force may be the magnetic field of a rotating magnetized neutron star, and (ii) the HII regions around rotating magnetic Ap stars. I have considered this process elsewhere (unpublished work) and found that the energy input in this case may be somewhat in excess of 10^{-27} erg $\text{cm}^{-3} \text{s}^{-1}$.

I thank Dr E. P. J. van den Heuvel for comments.

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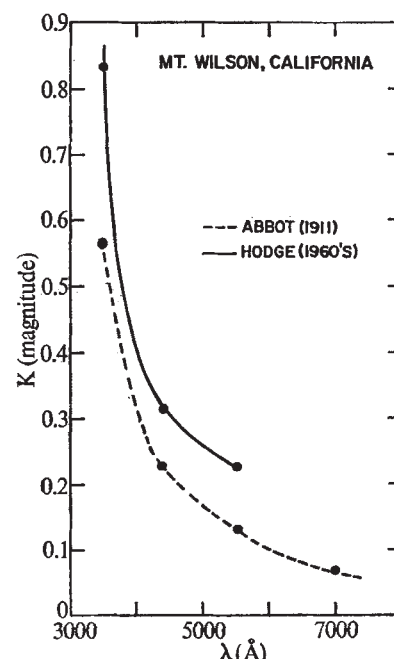


Fig. 1 A comparison of clear air extinction coefficients (in astronomical magnitudes) for the Mount Wilson Observatory for a period before 1911 and for nights in the years 1960–1962.

Large Decrease in the Clear Air Transmission of the Atmosphere 1.7 km above Los Angeles

ASTRONOMICAL measures of atmospheric extinction, routinely carried out during most programmes of astronomical photoelectric photometry, provide a large sample of data of importance to studies of long term anthropogenic pollution of the atmosphere¹. We have therefore begun an exhaustive compilation of present and past measures of extinction at as many observatories throughout the world as possible. I wish to point out one of the most important results so far, the measurement of a large secular decrease in the transmission of the atmosphere measured at a significant altitude above the Los Angeles Basin.

In 1911, Abbott² published the results of his measures of the transmission at various wavelengths of the atmosphere above Mount Wilson, California, which is on the rim of the Los Angeles Basin, 1,742 m above and 11 km horizontally from the centre of Pasadena, and 25 km from downtown Los Angeles. Fig. 1 shows a plot of his data for four wavelengths, in the ultraviolet, blue, yellow and red, given in units of atmospheric extinction by magnitudes, as conventionally determined by astronomers³.

In the years just before the advent of frequent occurrences of smog at these altitudes, which became important beginning in about 1962, I measured the atmospheric extinction in three wavelengths on 31 clear, smogless nights at the Mount Wilson Observatory. Measures were made in the standard way with photoelectric photometers attached to the 60 inch and 100 inch telescopes. The mean extinction coefficients are also plotted in Fig. 1, where they are compared with Abbott's values found just over 50 yr previously.

The differences in the extinction coefficients are striking: 0.27 mag. in the ultraviolet, 0.09 mag. in the blue and 0.10 mag. in the yellow. These are large differences, especially considering that the data for the 1960s were taken only on nights when

no trace of smog was detectable by tests for transmission variability. The fact that the early data are for daytime and the latter data are for night-time cannot conceivably account for this difference.

Table 1 gives the percentage decrease in the transparency that is indicated by these figures. It shows that the apparent secular change in the clear air transparency for this site, far above the Los Angeles Basin, is as large as 26% in the ultraviolet during this crucial period. This is clearly an important example of how astronomical current and archival data of this sort can be useful in studies of atmospheric aerosol pollution, which have taken on a recent urgency because of speculation on the possible effects on world climate^{4–6}.

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Table 1 Decreases in Atmospheric Transmission at Mount Wilson

Wavelength (μm)	50 yr decrease (%)
0.35	26
0.44	9
0.55	8

Shear Wave Propagation in Rocks

We have demonstrated striking similarities in elastic wave propagation through rocks and single crystals in recent experiments. In particular, we find that two shear waves with displacements perpendicular to one another and with differing velocities are often propagated through rocks. This is illustrated in Fig. 1 at 5 kb pressure for samples of slate and dunite; an ultrasonic technique described by Birch¹ was used. One MHz AC-cut quartz transducer generated and received the shear waves, and an electrical pulse of 50 V was used to excite

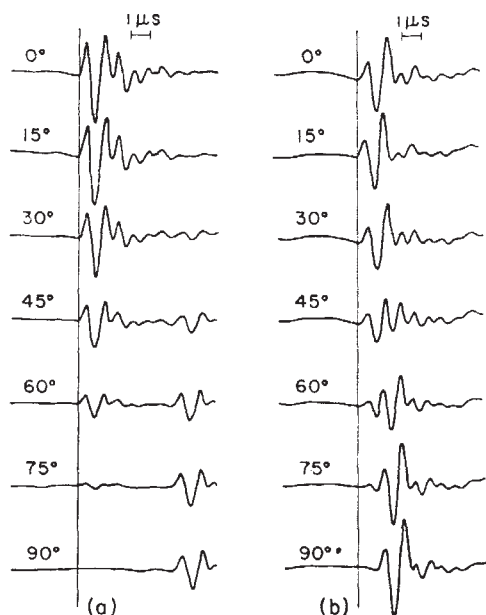


Fig. 1 Oscilloscope traces for shear wave propagation through (a) slate from Poultney, Vermont, and (b) dunite from Twin Sisters Peaks, Washington. The transducers are oriented at 0° to receive the higher velocity shear wave. Rotation of the transducers through 90° emphasizes the first arrival of the slower of the two shear waves.

the transducers. The rock samples were cylinders 2.54 cm in diameter and approximately 6 cm long.

For the slate the propagation direction of the shear wave was parallel to the cleavage. The transducers were rotated in steps of 15° such that shear waves were first propagated with a displacement direction parallel to the cleavage. Fabric study of the dunite shows a strong concentration of olivine a crystallographic axes and girdles of b and c axes. Propagation in the sample shown in Fig. 1 was normal to the a axes concentration.

Two shear waves with differing velocities are obviously propagated through both rocks. Velocities for the two shear waves in the slate differ by approximately 1 km s^{-1} , whereas velocities of the two waves in the dunite differ by 0.3 km s^{-1} . The latter value seems to be quite typical for shear velocity anisotropy in dunites. The phenomenon is common in metamorphic rocks and has been observed in several igneous rocks. The time resolution did not always permit clear identification of the two shear waves, but a rotation of the transducers produced a change in shape of the first arrival which strongly suggests the presence of this type of anisotropy. In all cases the observed anisotropy seems chiefly to be the result of preferred mineral orientation.

The importance of this study for shear wave propagation within the Earth remains to be established. The recognition of two shear wave arrivals would, clearly, provide unequivocal evidence for seismic anisotropy in regions of the upper mantle where longitudinal waves appear to vary in velocity with azimuth. It is highly probable that many regions of the Earth's crust and mantle are anisotropic and, hence, two shear waves should be propagated through these regions. It is possible that the arrival of one of the shear waves is often masked by the arrival of other energy.

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Measurement of Tilt of a Frozen Sea

IN May 1967, as part of a programme of geodetic studies in the vicinity of the North Pole, an attempt was made to measure the tilt of the fluid surface of the Arctic Ocean. Three holes were drilled through the ice and the tilt relative to the equipotential surface was determined by levelling from hole to hole with a levelling instrument¹. Two sets of observations were taken at a distance of about 56 km from the North Pole on May 11 and 13, 1967. Both measurements showed a downward tilt of 8 ± 2 seconds of arc in the direction of 100° and 150° west of Greenwich, respectively. This experiment showed that, if the measurements are correct, large ocean tilts in the polar region may occur. However, because of atmospheric refraction, this technique is not suited for the desired degree of precision and the search for a better method led to the development of a hydrostatic levelling system that was tested in the vicinity of the North Pole in April and May 1969 and in the Gulf of St Lawrence in March 1970².

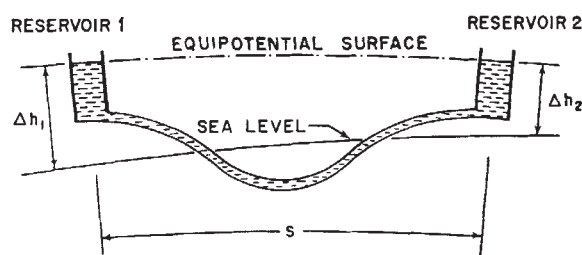


Fig. 1 Schematic diagram of hydrostatic levelling system.

The tilt α is $\frac{\Delta h_1 - \Delta h_2}{s}$. The instrument dimensions are: tube length 120 m, tube diameter 1.27 cm, reservoir height 12 cm and reservoir diameter 4.6 cm. The system is filled with a low viscosity silicone fluid.

Fig. 1 illustrates the system schematically. Two water wells are formed by drilling and freezing electrically heated, insulated pipes into the ice, 120 m apart. The hydrostatic level consists of two reservoirs bolted to the wells and connected by a horizontal tube. The usual problems associated with hydrostatic levelling systems required that the tube is positioned as nearly horizontal as the terrain allows. The system is filled with a low viscosity silicone fluid. If it is not moving, and under conditions of equal atmospheric pressure at the wells and constant fluid temperature throughout the system, the fluid surfaces in the two reservoirs form part of the same equipotential surface. If Δh_1 and Δh_2 are the level differences between the fluid levels of the reservoirs and the ocean surface and s is the separation between the two reservoirs, then the tilt is $\frac{\Delta h_1 - \Delta h_2}{s}$. The level difference $\Delta h_1 - \Delta h_2$ is determined by

measuring the level differences f_1, w_1, f_2, w_2 relative to a level plate using pointed measuring rods connected to micrometers. The sensitivity of the system is given by the ratio of the smallest fluid level difference $\Delta h_1 - \Delta h_2$ that can be measured, and the level length s . External effects, listed below, cause a displacement of the fluid levels, contributing to an apparent tilt if not monitored and corrected for. In developing the system we attempted to keep the measurement of the level difference $\Delta h_1 - \Delta h_2$ within a standard deviation of $\pm 2 \times 10^{-5} \text{ m}$, resulting, with a level length of $s = 120 \text{ m}$, in a sensitivity of $\pm 1.6 \times 10^{-7}$ radians. The threshold values of external error sources above which corrections have to be applied (Table 1) are therefore reached when the resulting level displacements exceed $\pm 1.0 \times 10^{-5} \text{ m}$.

(1) As long as the connecting tube is perfectly horizontal only the temperature differences of the fluid between the two reservoirs matter. It is measured to an accuracy of $\pm 0.01^\circ \text{ C}$ using thermistors. (2) The possibility of density changes of the

seawater in the wells is avoided by pumping the old water out of the wells before each measurement. (3) Atmospheric pressure gradients in excess of $30 \mu\text{bar km}^{-1}$ are rare. (4) V_1 and V_2 are the current speeds of the water flowing past the bottom openings of the wells which cause a pressure decrease in the wells. The Bernoulli effect is insignificant for current speeds of less than 8 cm s^{-1} . During periods of rapid drift the flow rate must be measured with current meters. (5) The component of the acceleration in the direction of the level axis and (6) the velocity component at right angles to the level axis must be considered. The system is made insensitive to vertical accelerations (wave motions) by choosing its dimensions such that the dynamic response of the level fluid is critically damped.

The pack ice commonly drifts at speeds and accelerations which are a magnitude larger than the threshold values. Therefore of all external effects, the system is most sensitive to drift speed and accelerations. Precise navigation is therefore a prerequisite to precise tilt measurements.

Table 1

Error source	Threshold value
1. Temperature of the hydrostatic fluid	$\pm 0.06^\circ \text{C}$
2. Density change of the well water	$\pm 5 \times 10^{-6} \text{ g cm}^{-3}$
3. Atmospheric pressure gradient	$30 \mu\text{bar km}^{-1}$
4. Differential flow (Bernoulli effect)	$V_1^2 - V_2^2 < 2 \text{ cm}^2 \text{ s}^{-2}$
5. Horizontal accelerations	$1.6 \times 10^{-4} \text{ cm s}^{-2}$
6. Drift velocity (Coriolis force)	1.1 cm s^{-1}

Table 2

	Level I	Level II
Date	April 30/69	May 2/69
Position	$89^\circ 29.2' \text{ N}$, $31^\circ 30' \text{ W}$	$89^\circ 25.0' \text{ N}$, $21^\circ 00' \text{ W}$
Time (GMT)	0200	2200
Drift speed (cm/sec, constant)	5.6	1.8
Direction of drift	300°	56°
Direction of level axis	248°	129°
Observed tilt*	4.71 ± 0.07	3.15 ± 0.08
True tilt (Coriolis corrected)*	5.22 ± 0.07	3.23 ± 0.08

* Down-slope in direction of level axis, in units of micro-radians.

The results of the tilt measurements near the North Pole determined with two hydrostatic levels are listed in Table 2. Directions are west of Greenwich. The observed tilt has been calculated from the mean of 40 measurements of the level differences f_1, f_2, w_1, w_2 (Fig. 1) after corrections for the temperature changes of the reservoir fluids had been applied.

Tilt observations in the Gulf of St Lawrence were carried out in an area between Amherst Island and the eastern tip of P.E.I. The sea surface sloped down in a northerly direction. Preliminary results show that the observed tilt ranges from -0.4 to 3.5 micro-radians².

We have shown an experimentally tested method which allows us to measure the tilt of a frozen ocean with high accuracy. We believe that it is important, from both geophysical and oceanographic points of view, to use automatically recording sensors of this type over baselines which are of the order of 10^2 km to determine the extent and persistence of ocean tilts. As part of a proposed international study of ice deformation, known as Arctic Ice Dynamics Joint Experiment, it is hoped to set up four pairs of sensors at the corners of a 100 km square with an additional pair in the centre. These would permit the statistical calculation of planar, quadratic and cubic tilt surfaces with varying degrees of overdetermina-

tion, since there will be ten distinct measurements of ocean tilt at these five stations.

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Baffin Bay—an Ocean

RECENT theories of the opening of the Atlantic Ocean and the Labrador Sea and of the relationship of the assumed motions to the history of Baffin Bay lead to contradictory opinions about the nature of the crust beneath the bay. The fit of the continents¹ and the similarities of the rock types and their ages along the opposing coastlines of Greenland and Northern Canada^{2,3} suggest that the two have separated by continental drift. Geophysical studies in the Labrador Sea (unpublished work of X. Le Pichon, R. D. Hyndman and G. Pautot) imply that Baffin Bay was formed by seafloor spreading and therefore that oceanic crust should lie beneath it. Conversely, from an interpretation of the geology along the coastlines, the present configuration of the bay has been attributed to the extension of continental material and subsequent faulting among its margins⁴. The latter hypothesis is supported by a study of

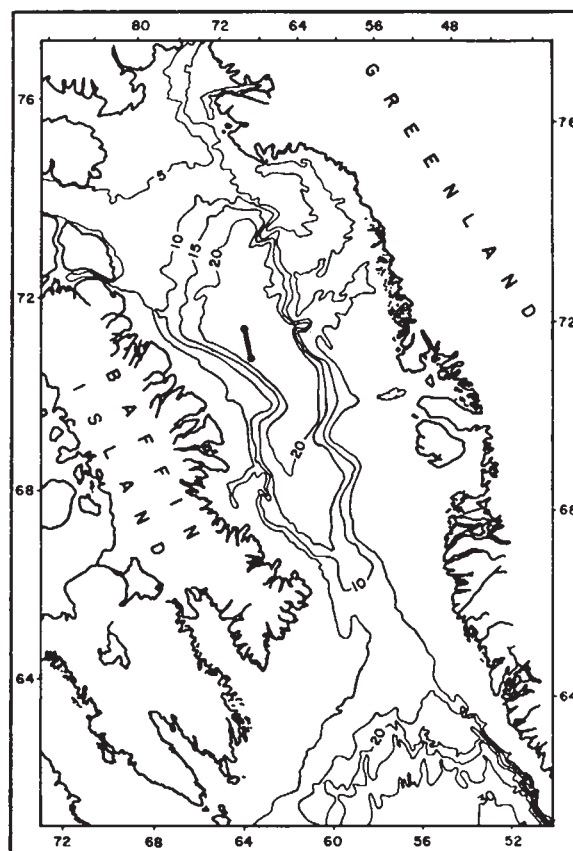


Fig. 1 Location of the refraction line (the heavy black line). The bathymetry contours are in hundreds of metres.

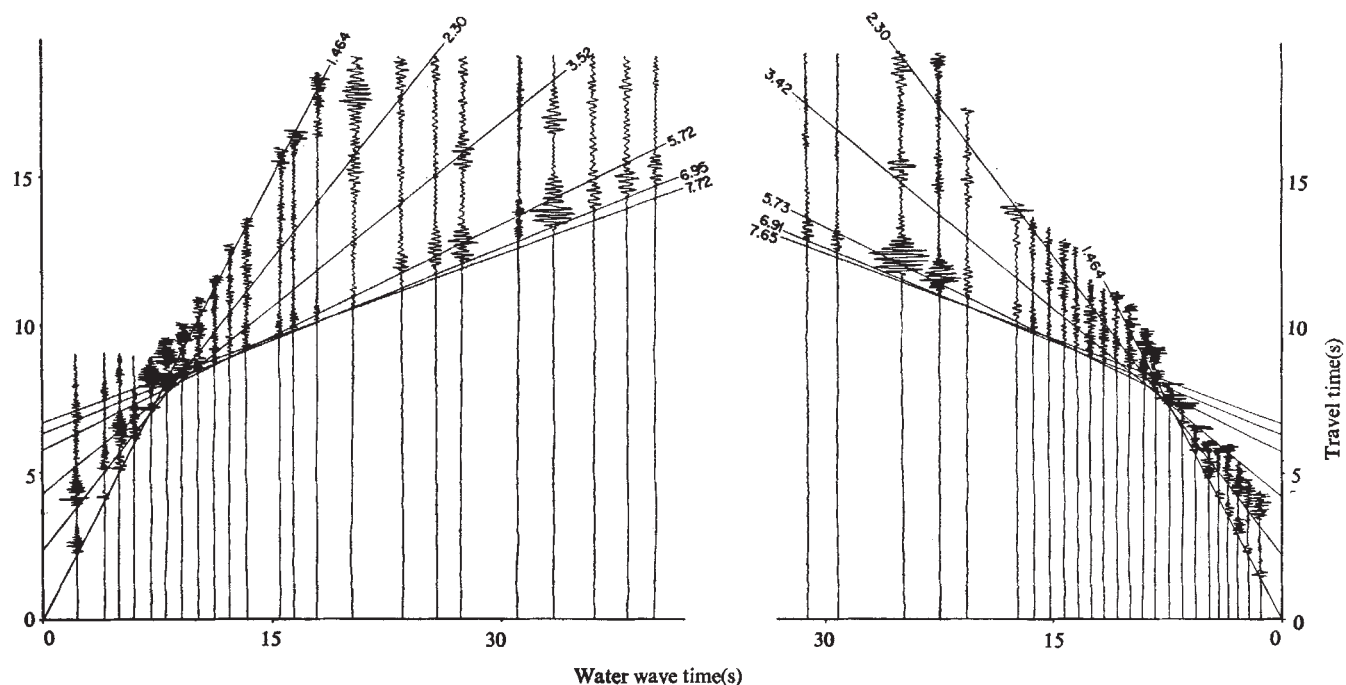


Fig. 2 The record stations. Velocities are in km/s. The right-hand figure shows recordings at the southern station and the left-hand figure shows recordings at the northern station.

surface waves⁵ which showed that the Lg phase is transmitted across the area. This surface wave is generally associated only with continental crustal structure. The lack of any positive evidence which could be used to resolve this controversy prompted us to conduct the experiment described here.

A two-ship seismic refraction line was performed in the deep region of Baffin Bay in October 1970 (Fig. 1). CSS Hudson acted as the recording ship and USCGC Edisto as the shooting ship. The line was reversed; however, the second shot line did not coincide exactly with the first due to ice conditions at the two ends of the proposed line. The two resulting shot lines did not diverge by more than 18 km. Also, Hudson drifted about 12 km and 6 km respectively at the southern and northern receiving stations during the listening periods. The positions of the shot lines were determined by LORAN navigation and the location of the receiving stations by satellite fixes. The explosive charges were fused fired and the charge sizes ranged from 30 to 500 pounds (13 to 230 kg).

Corrections were applied to remove variations in the travel times due to bottom topography along the shot lines and beneath the receiving stations. The constant water depth to which all travel times have been corrected is 2.30 km. Shot to receiver ranges were obtained from the direct water wave arrivals using a velocity of 1.464 km/s for sound in seawater. This value was calculated from previous measurements of temperature and salinity in central Baffin Bay⁶. Recordings of all shots were appropriately arranged and are presented as record sections in Fig. 2.

Five crustal velocities are shown on each record section. The velocities of 7.7 km/s and 6.9 km/s are well established, the former by first arrivals and the latter by good second arrivals. The 5.7 km/s velocity is defined by first arrivals over a small distance interval—this is best seen on recordings at the northern station. The values of the two lower velocities, 2.3 and 3.5 km/s, have been assumed; however, their values are not critical to the results reported here.

True velocities and the layer thicknesses were calculated and these are shown in Table 1. The velocities, 5.7, 6.9 and 7.7 km/s, are similar to those measured for layers 2 and 3

and the M discontinuity respectively in the ocean basins⁷, and we shall use this terminology in the following discussion. The total depth to the M discontinuity from the sea surface is 11 km including 4 km of sediment. This depth and the layer velocities bear no similarity to continental crustal values but are closely related to those obtained in oceanic areas. There are, however, several differences. The unusually thick sedimentary cover is substantiated by reflexion profiling results, and in view of the landlocked nature of Baffin Bay a thick sequence of sediments is not unreasonable. The thickness of layer 2 is similar to that measured in the deep ocean basins but the thickness of layer 3 is appreciably less. If the deep central portion of Baffin Bay was formed by seafloor spreading, the lesser thickness of basaltic crustal rocks could be attributed to a different rate of outpouring of crustal material or to a different spreading rate than is at present observed at active ridges.

Table 1 Layer Thicknesses and Velocities

Layer	Velocity (km/s)	Thickness (km)	
		Southern station	Northern station
Water	1.464	2.3	2.3
Unconsolidated sediment	2.30	2.1	2.0
Sediment	3.47	2.0	2.3
Layer 2	5.72	2.0	2.1
Layer 3	6.93	1.9	2.1
Mantle	7.68	—	—

The positions of the southern and northern stations were 71° 39' N, 65° 55' W and 72° 18' N, 66° 13' W respectively. These are median positions taken during the time that Hudson was on station.

The velocity of the mantle rocks, 7.7 km/s, is slightly lower than that normally found in the ocean basins. It is not, however, significantly less than the mean measured beneath the Eastern North Atlantic basin⁷, for example, 7.85 km/s with a standard deviation of 0.18 km/s. Also, the mantle velocity may be lower because the M discontinuity is shallower

and the pressure less at the base of the crust here than in most other oceanic regions. Therefore, it would be unrealistic, though perhaps tempting, to attribute the low mantle velocity to "anomalous mantle" material often associated by some workers with mid-ocean ridges⁸.

In conclusion, both the thickness of the crust and the measured velocities show that the central deep portion of Baffin Bay is oceanic and that it cannot be attributed to extended and faulted continental material.

We thank the masters, officers, crew and the scientific parties of CSS Hudson and USCGC Edisto for their help. This work was part of the Hudson-70 expedition organized by the Atlantic Oceanographic Laboratory of Bedford Institute as a Canadian contribution to the International Decade of Ocean Exploration.

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Supernovae and the Extinction of the Dinosaurs

WE wish to suggest that a nearby supernova explosion might produce climatic effects so drastic as to cause the extinction of many animals, including the dinosaurs. Earlier discussions of this topic^{1,2} focused on the radiation doses to be expected as a result of the interaction of high-energy cosmic rays and γ -rays with the atmosphere. Reasonable estimates of the parameters involved implied doses which may account for some of the patterns of mass extinction observed in the geological record.

The belief that large fluxes of cosmic rays and γ -rays are produced during the early phases of a supernova outburst has been strengthened by the discovery of pulsars. In addition we might expect supernovae to be powerful emitters of soft X-rays during the first few days, as suggested by the identification of several features in the spectrum of type I supernovae as forbidden lines from highly stripped ions such as exist in the solar corona³. This requires that the expanding envelope have a temperature of the order of a million degrees, and suggests the existence of large X-ray fluxes. In general, if the efficiency of production of visible light relative to the production of high frequency radiation is small, of the order of a few per cent or less, then $\sim 10^{50}$ ergs in X-rays will be emitted in about a week as a result of a supernova outburst. It will soon be possible to verify or disprove the existence of large X-ray fluxes from supernova outbursts by satellite observations of supernovae in other galaxies⁴.

Estimates of the probabilities for nearby supernovae show that ~ 1 supernova explosion should occur within a distance of 100 light years every 50 million years¹. As a result of such an explosion, the atmosphere as a whole would absorb about 10^{28} ergs in X-rays in about a week or less, mostly in the

ozone layer and the ionosphere between about 20 and 100 km, depending on the spectrum of the radiation. This is a hundred times the far ultraviolet and X-ray flux received from the Sun during a week⁵.

The climatic effects of an enormous deposition of energy into the upper atmosphere are difficult to assess. London⁶ has suggested that heating at the top of an atmosphere produces ascending motions in the stratosphere which make the lower atmosphere unstable or aid in the vertical exchange of momentum. Sudden increases in the short wavelength ultraviolet and X-ray emission from the Sun have been followed after a few days by a shift of the atmospheric circulation toward a pattern with definite glacial characteristics⁷. In our case the effect must be catastrophic, for the energy deposited in the upper atmosphere is of the same order as the gravitational binding energy of that part of the atmosphere above 60 km. It is also of the same order as the total kinetic energy of the atmosphere⁸. Thus, we can expect that the entire atmospheric circulation system will be profoundly modified. This will undoubtedly have disastrous short term effects with many storms of extreme intensity generated.

Willett⁹ has speculated that climatic changes in general, and the ice ages in particular, are the result of significant variations of the ultraviolet emission of the Sun. The variation under discussion here is of a short duration, but because of its extraordinary intensity it may have long term ($\sim$ years) effects through a change of the albedo resulting from the formation of very high altitude ice clouds, or the alteration of the greenhouse effect due to the disruption of the ozone layer and the general large scale mixing of the atmosphere. Long term effects seem to be predominantly of a kind that produce increased storminess and lowering of temperatures over much of the Earth.

These effects are not necessarily unique to a supernova explosion. An intense source of high energy radiation is all that is required. Another possibility is an anomalously large solar outburst.

Although disputed by some^{11,12}, the latest Cretaceous and earliest Tertiary (Maestrichtian and Danian stages) have generally been recognized as a brief interval during which many organisms underwent a severe attenuation in diversity or became extinct^{13,14}. Among these were phytoplankton¹⁵, planktonic foraminiferids¹⁶, many forms of bivalve and cephalopod molluscs¹⁷, echinoids¹⁷, mosasaurs, plesiosaurs, marine turtles and dinosaurs¹⁸.

Typically Mesozoic marine faunas are found above erosional paraconformities ("hard grounds") in Maestrichtian carbonate deposits in Europe¹⁹ and the latest Cretaceous "Lancian" dinosaur fauna persisted through the time of maximum development of the Hell Creek floodplain in the western interior of North America, so that restrictions of epicontinental seas did not cause a serious attenuation of Mesozoic biota. Impoverished Danian faunas are, however, often separated by a bedding plane from Cretaceous faunas of similar sedimentary facies, and Newell's²⁰ implication that the intervening extinctions may have lasted considerably less than a million years seems to be reasonable.

It has been suggested that dinosaurs were gradually declining in taxonomic diversity during the latter part of the Cretaceous. This cannot be demonstrated because of the much smaller sample of Lancian dinosaurs relative to available specimens of Campanian forms²⁶, a lack of careful systematic studies of the groups, and limited area of the Earth from which the extrapolation is essentially founded (western interior of North America). Even if a decline should be documented in this region, a gradual climatic deterioration correlated with the southward shift of climatic zones, rise of Laramide ranges to the west and withdrawal of the interior sea may account for faunistic changes and yet not be linked to the causes of the extinctions at the close of the Cretaceous. Although ichthyosaurs probably declined to extinction before the end of the Cretaceous (ref. 27 and field records of the American

Museum of Natural History), and ammonites suffered a marked decline during the latter part of the period¹⁷, neither phenomenon seems to be directly linked to the extinctions at the Cretaceous-Tertiary boundary.

The globally depauperate Danian biota¹³, characterized by forms of a boreal aspect even in low latitudes²¹, suggest that a temperature drop was involved in the extinctions at the end of the Cretaceous. Lowenstam and Epstein's²² observation that water temperatures in Denmark during the lower Maestrichtian and upper Danian were similar implies that any such cool interval would have been short. Nagappa's²³ suggestion that "... a sudden though short lived cold period, not necessarily intense enough to bring about an ice age, was the cause of (the extinctions terminating the Cretaceous)", is not precluded by existing palaeobiological evidence.

In summary, the biostratigraphic record does not provide compelling support for considering global regressions of epicontinental seas or long term climatic trends as causative of the extinctions at the close of the Maestrichtian. It does suggest that the extinctions were of unusual magnitude and geologically brief duration, and may have been accompanied by a thermal drop. Eroded surfaces capping marine Maestrichtian sediments in stable tectonic areas may have been produced contemporaneously with the extinctions.

The biota of the Earth, which had not experienced widespread rigorous conditions for perhaps a hundred million years, probably would not have adjusted to the sudden onset of cool conditions as well as the modern biota. The disturbance of thermal stratification in the oceans by initial atmospheric turbulence, followed by several years of depressed temperatures, would dampen primary production in the oceans, concomitantly exterminating many forms in higher tropic levels²⁴. Atmospheric turbulence in conjunction with normal tidal currents may have results in the erosion of bottom sediments in many areas²⁵, thereby accounting for the widespread occurrence of a paraconformity separating Maestrichtian and Danian sediments in otherwise complete stratigraphic sections.

The supernova theory does not conflict with the record of extinctions at the Cretaceous-Tertiary boundary as at present understood. It has merit in that its predicted effects can be compared to the record to a greater extent than some other theories of mass extinction.

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BIOLOGICAL SCIENCES

Isolation of the Cholinergic Receptor Protein of *Torpedo* Electric Tissue

LEE and his co-workers have reported¹⁻³, and we have confirmed, that α -bungarotoxin (α -BuTX), a component of the venom of a Formosan snake (*Bungarus multicinctus*), blocks specifically and irreversibly the depolarizing action of acetylcholine at vertebrate neuromuscular junctions. We wish to report that this toxin similarly blocks the cholinergically innervated electric tissue of *Torpedo marmorata*, and to describe isolation of the single membrane protein to which the toxin is bound.

The electric tissue of *Torpedo* was chosen as a source of cholinergic receptors because of its special structure^{4,5} and its extraordinarily rich cholinergic innervation^{6,7}. Each electric organ is composed of about 500 columns of electroplaques, and each column has hundreds of cells. Judging

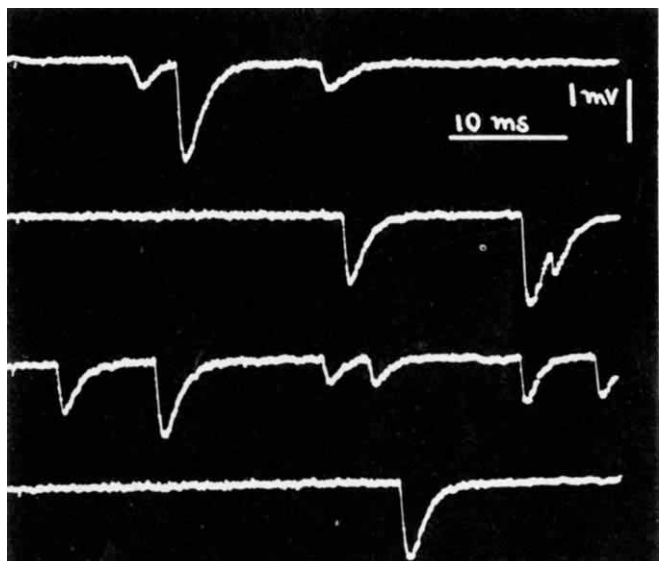


Fig. 1 Miniature synaptic potentials recorded extracellularly from an isolated piece of electric tissue. The potentials are a consequence of multimolecular amounts of acetylcholine acting on the membrane of an electroplaque, at about 23° C.

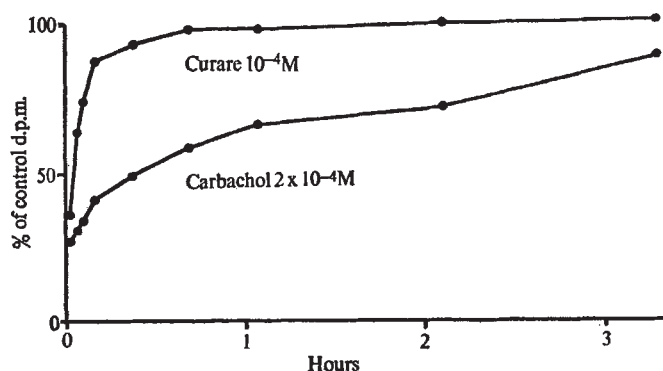


Fig. 2 Effect of d-tubocurarine and carbamylcholine on the binding of α -bungarotoxin to isolated membranes. Membranes from approximately 200 mg of electric tissue were incubated at 20° C in 1 ml. of buffer with or without the drugs indicated for 1 h, and then with 0.5 μ g/ml. of 125 I- α -bungarotoxin in addition for the times shown. The membranes were washed twice by sedimentation at 20,000g for 1 min and resuspension in fresh buffer, before being dissolved in an alkaline solvent for liquid scintillation spectrometry.

from freeze-etchings in which the fracture plane was that of the synaptic cleft (Nickel and Potter, unpublished; compare ref. 5), these thin flat cells are innervated over a large part of their ventral surfaces; and because of grooves and infoldings in the postsynaptic membrane, it seems reasonable to consider that the area of postsynaptic membrane is comparable with the total "flat" ventral cell surface. In the fresh organs of one small fish we have estimated that there were an average of 13,000 plaques per gram of tissue having a combined "flat" ventral cell surface area of 0.07 m². The tissue is thus an excellent source of postsynaptic membrane proteins.

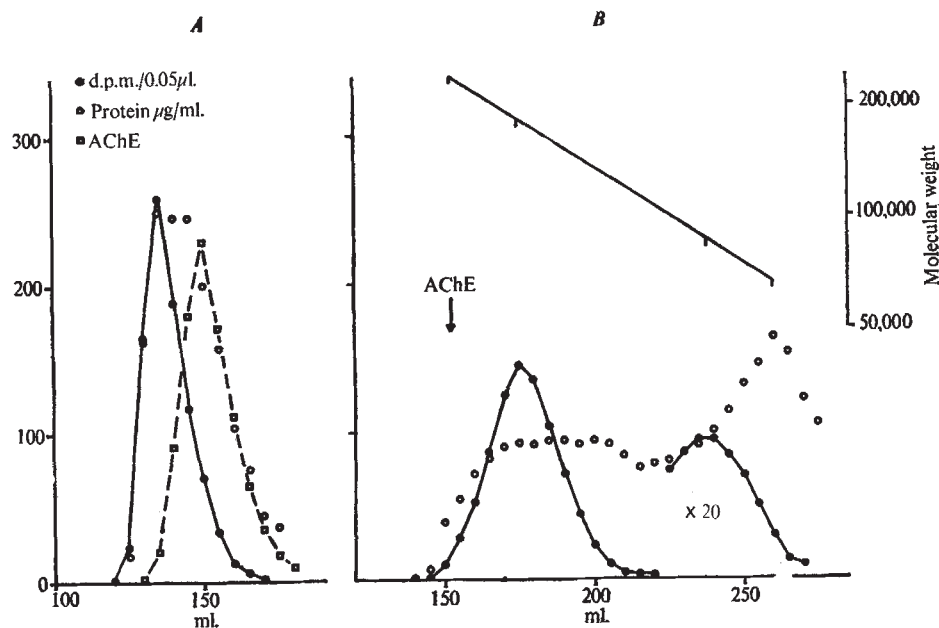
Twelve pure proteins were isolated from the dried venom of *B. multicinctus* by molecular sieving on 'Sephadex G-50' and cation-exchange chromatography on 'CM-Sephadex' (Miledi and Potter, unpublished). Four, including α -BuTX, blocked the action of acetylcholine on neuromuscular junctions in the frog sartorius; six blocked transmitter release from the motor nerves; one was acetylcholinesterase (AChE), and one was inactive at these junctions. To measure small amounts of bound toxin, the pure protein was labelled⁸ with carrier-free 125 I at initial specific activities of 23,000 Ci/mol (8,000g) of toxin.

As at other cholinergic synapses, the nerve terminals to

electroplaques release acetylcholine in multimolecular packages, and these "quanta" react with receptors in the postsynaptic membrane, evoking miniature synaptic potentials (Fig. 1). These potentials were used to examine the action of α -BuTX on the organ. For this purpose blocks of tissue with columns 2–8 mm high were exposed to the toxin (10^{-5} to 10^{-4} g/ml.) in elasmobranch Ringer. Miniature potentials were soon abolished in the superficial electroplaques, but it required 4 days' exposure at 4° C to 10^{-4} g/ml. to abolish miniature potentials in all the plaques of blocks 5 mm thick. Toxin-blocked electroplaques had normal resting potentials, and were insensitive to acetylcholine applied ionophoretically. In contrast, pieces of tissue kept without the toxin still had miniature potentials even 6 days after isolation. Thus it seems that in the electric organ of *Torpedo*, as at neuromuscular junctions, α -BuTX acts by blocking acetylcholine receptors. D-Tubocurarine (10^{-4} g/ml.) also abolished miniature synaptic potentials, and it required about 2 days to affect deep electroplaques. It is interesting to note that even massive injections of curare to the fish, including intra-arterial administrations, are known to act slowly in this tissue^{9–11}.

Because of the difficulty of applying the toxin to cells in intact tissue, subsequent studies were carried out with disrupted cells. Preliminary experiments indicated that postsynaptic membranes (identified by their content of AChE) could not be cleanly isolated from other cell membranes by density gradient centrifugation. The following procedure was therefore developed to isolate most of the total membrane content of the tissue, without large losses of AChE. Electric organs were homogenized with four times their weight of 0.4 M NaCl in a Waring blender operating at top speed for 2 min. The homogenate was poured through a sieve to remove fragments of connective tissue larger than 0.3 mm, and was centrifuged at 23,000g_{max} for 15 min. The pellet was vigorously resuspended and osmotically shocked in 20 mM sodium phosphate, pH 7.5 ("buffer": 1 ml./g of original tissue), with the aid of a Polytron blender operating at 22,000 r.p.m. for 1 min. This suspension was recentrifuged and the pellet was resuspended as before. Electron micrographs of the particles showed a wide range of sizes of membrane fragments and large vesicles. One gram of tissue was found to have 23.5 mg of protein¹², of which 5.6 mg, or 24% of the total, was recovered with the isolated membranes. The corresponding recovery of AChE (ref. 13) was 82% of 0.78 mmol acetylthiocholine hydrolysed per min. Assuming a molecular weight of 240,000 for the enzyme, four active sites per molecule, and an activity of 12.5 moles acetylcholine hydrolysed per min per gram (ref. 14), there are 62 μ g, and

Fig. 3 Chromatography of toxin-labelled protein at 4° C on a 450 ml. column of 'Sephadex G-200' in 20 mM buffer. Membrane proteins were dissolved in 1.5% 'Triton' after partial labelling of cholinergic receptor protein on the membranes with 125 I- α -bungarotoxin. Results in A were obtained in the presence of 1.5% 'Triton'. Results in B were obtained with 1% 'Triton' and 0.5% SDS after the addition of 10 mg of bovine serum albumin. AChE activity is given as μ mol acetylthiocholine hydrolysed/min/10 ml.; a trace of activity was noted in SDS in the position indicated. At the upper right, a plot of log molecular weight against peak elution volume between AChE (240,000) and albumin (67,000) indicates that the toxin-labelled protein moved in SDS as would globular proteins having molecular weights of about 180,000 and 88,000.



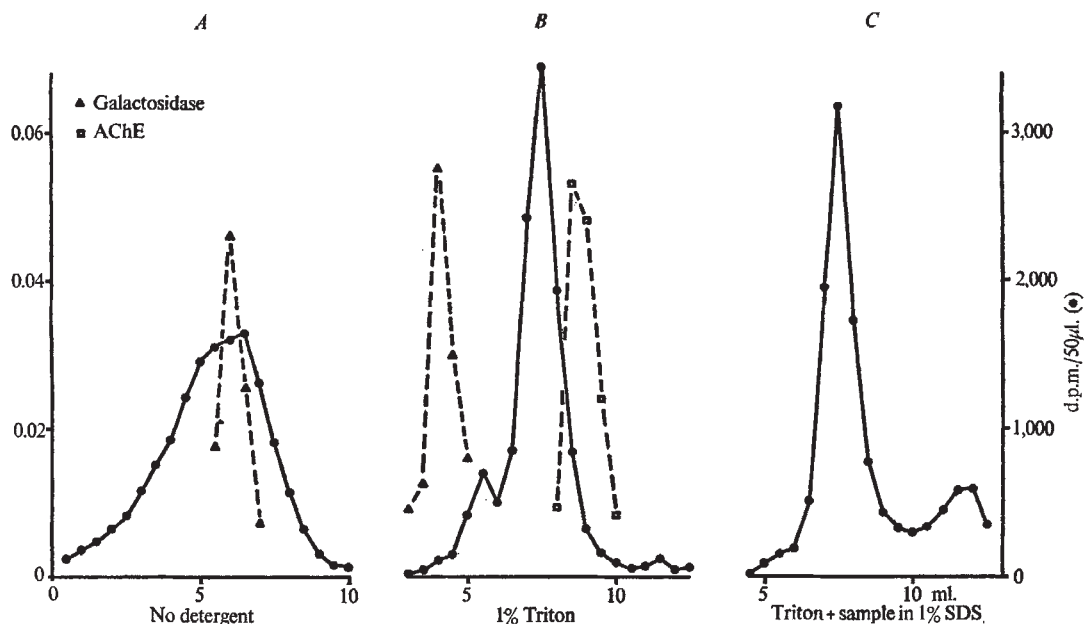


Fig. 4 Ultracentrifugation of toxin-labelled protein. Samples from the peak fraction of 'Sephadex G-200' in 1.5% 'Triton' (Fig. 3A) were diluted to 0.5 ml. with 50 mM Tris-HCl, pH 8, in 50 mM KCl-0.1 mM EDTA, and a small amount of β -galactosidase was added where indicated. The samples were centrifuged into linear density gradients of glycerol prepared in the same solution (12 ml., 10–30% glycerol v/v, in Spinco SW 40 Ti tubes), at 3°C for 15 h at 37,000 r.p.m. (A) or for 22 h at 39,000 r.p.m. (B and C). AChE activity is given as μ mol of acetylthiocholine hydrolysed/min/ml., and β -galactosidase activity is the change in absorbance at 420 nm/min when 20 μ l. of the gradient solution was added to 3 ml. of 2 mM *o*-nitrophenyl- β -D-galactopyranoside in 100 mM sodium phosphate, pH 7.5. The horizontal scales show the number of millilitres from the bottom of each centrifuge tube.

6.3×10^{14} active sites of AChE per gram of tissue. When 5 μ g of ^{131}I - α -BuTX was added to homogenates of 1 g of tissue, the recovery of ^{131}I in the final membrane suspension was 85%.

Binding of the labelled toxin to isolated membranes was found to be dependent on the concentration of the toxin and on time, and was saturable. When the membranes from 1 g of tissue were exposed to 200 μ g of toxin in 10 ml. of buffer at 4°C, the amount of toxin remaining bound to twice washed membranes (washed by sedimentation and resuspension in fresh buffer) was 7.43 μ g, whether the exposure was for 1 min or 1 h. Allowing for 85% recovery of the toxin binding sites of the tissue, in the membrane suspension, there seem to be 6.6×10^{14} binding sites per gram of tissue. This corresponds to 5.0×10^{10} sites per cell (the small cells measured), and to roughly 10,000 sites/ μm^2 of postsynaptic membrane. Binding of the toxin was slowed by d-tubocurarine, a competitive antagonist of acetylcholine at the receptors, and was slowed by carbamylcholine (Fig. 2). The rate of binding of the toxin also seems to be reduced at neuromuscular junctions which have been desensitized by acetylcholine (Miledi and Potter, unpublished), suggesting that the toxin does not bind effectively to desensitized receptors. This may explain the more pronounced effect of carbamylcholine than d-tubocurarine seen in Fig. 2. Carbamylcholine slowed binding of the toxin to the solubilized receptor protein (discussed later) to a similar degree, for example, by 50% in 10 min with 2×10^{-4} M carbamylcholine. Neither physostigmine, 10^{-4} M, nor 1% sodium dodecyl sulphate (SDS) had any observable effect on the amount of binding in 10 min. For these latter experiments excess labelled toxin was separated from the toxin-receptor complex on 1 ml. columns of 'Sephadex G-50'.

Several means for dissolving membrane proteins were investigated. Some partially (2 M NaBr) or fully (8 M urea) dissociated the toxin from the receptor, and others (including 2 M NaI) prevented subsequent binding of the toxin to dialysed, soluble proteins. The non-ionic detergent, 'Triton X-100', proved most satisfactory in that it quantitatively dissolved the receptor or receptor-toxin complex and AChE, and permitted the same amount of binding of the toxin to the soluble receptor

as was seen with the membranes. For the following experiments the membrane-bound receptor was partially labelled with ^{131}I - α -BuTX, dissolved in 1.5% 'Triton' (w/w in buffer; 30 min at 4°C), and remaining membrane material was removed by centrifugation at 100,000g for 1 h. Soluble membrane proteins averaged 8% of the tissue protein.

The toxin-tagged protein was characterized as follows. On 'Sephadex G-200' (Fig. 3A) it was eluted in the void volume, accompanied by about 20% of the soluble membrane protein, and before AChE, indicating a molecular weight greater than that of the esterase. In contrast, when the sample and column contained SDS, the labelled protein moved in two peaks as would globular proteins having molecular weights of about 88,000 and 180,000 (Fig. 3B).

Ultracentrifugation in density gradients containing 1% 'Triton' showed that the toxin-labelled protein sedimented primarily in one peak (Fig. 4B) between the smaller marker, AChE, and a polymer of β -galactosidase from *E. coli* known to have a molecular weight of 600,000–650,000 (personal communication from P. Butterworth). Variable amounts of a somewhat larger labelled protein were always present. Without 'Triton', the labelled protein aggregated into forms which sedimented in the range 0.5–2 million (Fig. 4A); whereas when the toxin-receptor was pretreated with 1% SDS, and then centrifuged into a gradient containing 1% 'Triton' without SDS, both smaller units and the re-aggregated primary form were seen (Fig. 4C).

Preliminary studies of the binding of ^{131}I - α -BuTX to nearly pure samples of the soluble receptor protein (obtained by ultracentrifugation in 6–20% sucrose gradients containing 1% 'Triton') indicate a ratio of approximately 1 μ g of toxin bound to 10 μ g of protein.

From our results we can draw the following conclusions. (1) The acetylcholine receptor is a membrane-bound protein which is readily solubilized in an active state by 'Triton X-100'. (2) It is composed of units with a molecular weight of about 80,000, each of which seems to have one binding site for α -BuTX. These units aggregate into polymers, of which the primary form seen in 1% 'Triton' appears to be a tetramer having four binding sites. A hexamer would explain the

somewhat larger protein. In 0.5% SDS the primary form seems to be a dimer of these units. (3) The number of toxin-binding sites per gram of tissue is the same as the number of active sites of AChE, as has been reported by others¹⁵ for electric tissue from eels. It is interesting that if each protein has four active sites, the number of molecules of receptor and enzyme is also the same. The active enzyme and the receptor protein are clearly separable, however, and do not at present seem to have a common subunit.

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Can a Peripheral Retinal Ganglion Cell respond Differentially to Images in or out of Focus?

ALL modes of visual excitation are dependent on the state of focus of stimuli reaching the retina. A differential response by the ganglion cell to images in or out of focus is therefore necessary before further analysis by the visual system.

Of the 122 retinal ganglion cells and optic nerve fibres investigated in this study, those described were all recorded intrabulbarly following the procedure of Barlow *et al.*¹ In order to eliminate the effect of tapetum reflexion, most of the cells were recorded from non-tapetal areas of the retina, although cells in the tapetal regions were also found to behave in a similar manner to those in non-tapetal areas. Fourteen cats (average body weight 2.8 kg) were used. The animals were surgically prepared under an initial dose of 60 mg/kg thiopentone sodium BP 2.5% solution given intraperitoneally. During the experimental period (15–20 h), they were maintained on a mixture of gallamine triethiodide (5 mg kg⁻¹ h⁻¹) and thiopentone sodium (1.5 mg kg⁻¹ h⁻¹) in 5% dextrose-normal saline infused by a femoral vein cannulation at a rate of 5 ml. kg⁻¹ h⁻¹. They were artificially respired with a mixture of 95% oxygen and 5% carbon dioxide. The electrocardiogram and body temperature were monitored throughout. Tungsten micro-electrodes coated with a clear vinyl lacquer (tip size 0.5 µm or less) were used in conjunction with a conventional recording system. The pupils were maintained at a diameter of 10 mm with 10% phenylephrine hydrochloride (BPC) and 0.6% atropine sulphate. The eye was fitted with a contact lens (12 mm in diameter) and was refracted along the axis of

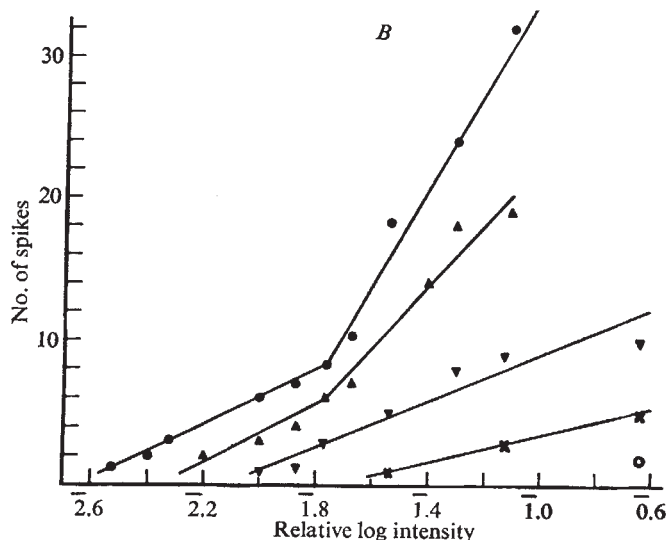
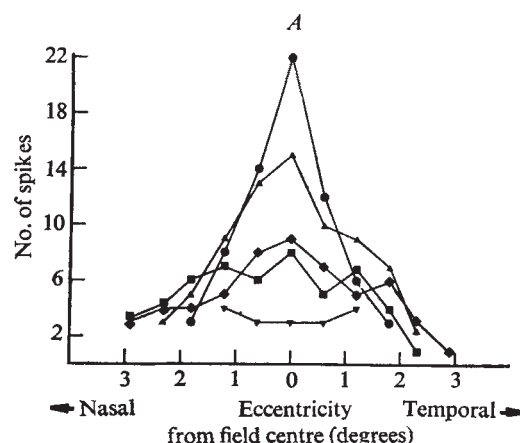


Fig. 1 A, Responses of a ganglion cell to a flashing spot stimulus (500 ms on/500 ms off) presented at local sites across a diameter of the receptive field when viewed through lenses of different refractive power. Although response curves were obtained for every other dioptric step from -4 to +20 dioptres, only representative curves are shown here. Corrections: ■, +16.00 dioptres; ▲, +12.00 dioptres; ●, +8.00 dioptres; ◆, +4.00 dioptres; ▼, -4.00 dioptres. B, Responses from the same sites as above in response to flashing (500 ms on/500 ms off) stimulus spot (28' of the visual arc) of different intensities (log 0=45 cd m⁻²) as viewed through a +8 dioptre lens (focused for 1 m). Background luminance=0.034 cd m⁻². Representative curves for nasal field sites are shown here. Curves for temporal sites are similar. Note the marked increase in sensitivity which develops at the field centre as the stimulus intensity reaches more photopic levels. ●, At field centre; ▲, 0.6° from field centre; ▼, 1.2° from field centre; ×, 2.4° from field centre; ○, 3.4° from field centre. This cell was located 34° temporal and 2° superior to the area centralis.

each receptive field by ophthalmoscopy and also retinoscopy. Further ophthalmic lenses were placed 12 mm in front of the eye concentric with each field axis to make the retina conjugate with the stimulus projection screen 1 metre from the eye, or to create selected degrees of refractive error. The stimulating light was projected upon the illuminated screen by the system described by Crawford and Ikeda². The combination of an eye ring sutured to the sclera and continuous infusion of gallamine triethiodide ('Flaxedil') stabilized the eye. Thus, the accommodative oscillations and microneystagmus normally in play are absent in our experimental conditions.

For each cell, the boundaries and the response geometry of the receptive field were plotted with the eye corrected for one metre. A photopic test spot (28' of the visual arc, 154.4 cd m⁻², 500 ms duration at 1 c.p.s.) was used as a standard for this

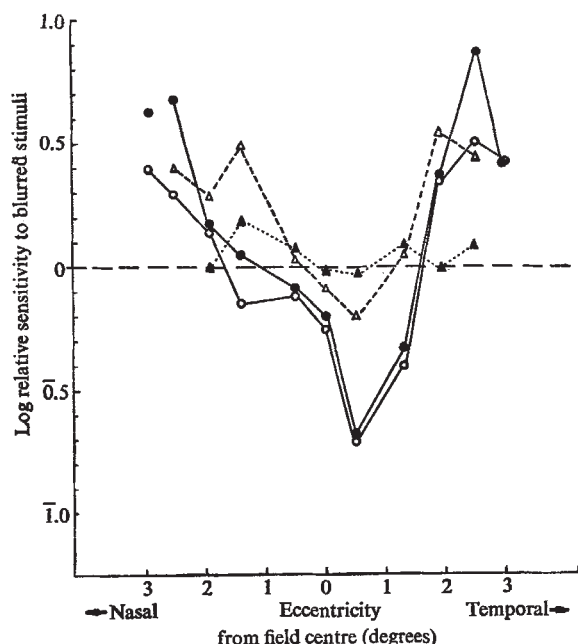


Fig. 2 Sensitivity at each of the field sites tested in Fig. 1A. The spike numbers were obtained with the standard spot intensity (4.802 cd m^{-2}) and with various blurring lenses in place, equated in each case with that focused stimulus intensity found for each site to produce the same spike number in Fig. 1B. Log 0 on the sensitivity scale is equated to 4.802 cd m^{-2} of focused stimulus intensity. The correction value given for each lens is its dioptric difference from the lens of best focus for 1 m (+8 dioptres). Only four representative curves out of thirteen obtained across the dioptric range explored (corrections from -12 to +12 dioptres) are shown here. Blurring corrections: $\circ$, +10 dioptres; $\triangle$, +4 dioptres; $\blacktriangle$, -2 dioptres; $\bullet$, -6 dioptres.

procedure against a background producing high contrast (0.034 cd m^{-2}). Local sites across the longest diameter of the receptive field were then replotted repeatedly and the spikes counted for each stimulation period. In the first condition, lenses of a range of refractive powers were used together with a test spot of reduced intensity (usually 1–1.5 log units below the 154.4 cd m^{-2} initially used), so that lateral interaction and light scatter would be negligible. Although we did not include the data in this communication, we have taken a series of retinal fundus photographs of the stimulus spot projected on the retina under focused and defocused conditions. The densitometer analysis of such photographs indicated that the light scatter is negligible (5% of the diameter of the spot of the retina). In the second, a wide range of spot intensities was used (usually a 3 log unit range) with the best refractive correction in place. This procedure made it necessary to record from a ganglion cell for 4–5 h. Fig. 1 shows a representative result obtained from a ganglion cell located in the peripheral retina whose receptive field projects into visual space, 34° nasal and 2° inferior to the visual axis. The cell responded vigorously to light "on" throughout the receptive field and only sporadically to light "off" at the field periphery, even in high contrast stimulus conditions and at photopic background levels.

In Fig. 1A, the number of spikes produced with the test light "on" at each location along the horizontal axis within the receptive field is shown for representative refractive conditions. To determine local thresholds without lateral interaction, a stimulus condition which evoked no "off" response was chosen. In Fig. 1B, the spike count as a function of log intensity of the stimulus spot is shown for each of those sites tested across the receptive field of the ganglion cell in the focused conditions. The relative sensitivity at each test site to focused compared with defocused stimuli was then determined by finding the focused test spot intensity from Fig. 1B which produced the same spike count as a given blurred stimulus at that site (Fig. 1A). The values for all sites tested are summarized in Fig. 2.

For focused images the threshold increases steeply away from the centre of the receptive field. The response is sensitive to changes of $15'$ of an arc or less, suggesting a critical centre favouring a directional mechanism even for visual fields 30° or more from the visual axis (see Fig. 1A, +8 DS curve).

Although out of focus stimuli of $28'$ of an arc or less may remain detectable over a considerable dioptric range (upward of ± 12 dioptres for the conditions used), directionalization based on the slope of the spike-distance curve deteriorates rapidly (see Fig. 1A, +12 and +4 DS curves). In extreme defocused conditions, the local thresholds may become so uniform across the field that the same spike number may be produced for a given stimulus anywhere within the receptive field (see Fig. 1A, +16 and -4 DS curves), thus permitting the maximal directional error in space (that is, equal to the radius of the field).

In defocused conditions, the cell responds rather more robustly to the stimulus when it is presented at the periphery of the receptive field than under the focused conditions; no light produces no response at all. Thus an apparent increase in peripheral sensitivity seems to occur (Fig. 2). Although the directional role of the cell is considerably diminished, it continues to detect quite effectively the presence of the diffuse image (see Fig. 1A, -4 DS curves).

The peripheral ganglion cell thus combines a large receptive field for the detection of diffuse images with a central organization favouring the localization of sharp images.

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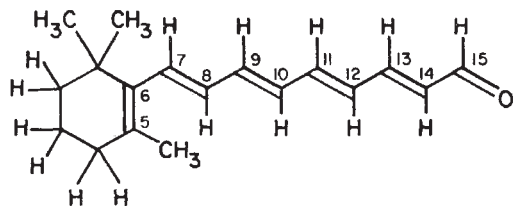
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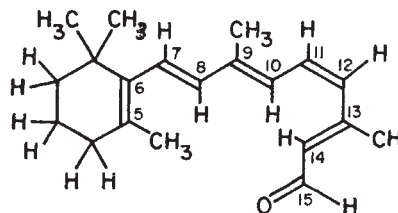
Implications of Torsional Potential of Retinal Isomers for Visual Excitation

BECAUSE 11-*cis* retinal is the chromophore of the visual pigment in vertebrate rods, and its isomerization to the all-*trans* form (Ia) is known to occur during visual excitation¹⁻⁴, the properties of the retinal isomers are of considerable interest. Although it has long been assumed that non-bonded repulsions in 11-*cis* retinal distort the polyene chain, the details of the ground state geometry have not been determined, nor has the experimental spectrum been correlated unequivocally with the excited states. In this communication, we present a theoretical ground state potential function with a form which may help to explain some of the unusual spectral characteristics of the retinal isomers when in solution or incorporated into the native visual pigment¹⁻⁴.

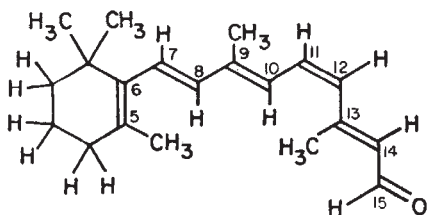
Fig. 1 shows the calculated potential energy of 11-*cis* retinal as a function of the $C_{12}-C_{13}$ torsional angle; the method is outlined in the figure caption⁵⁻¹⁰. A conformation in which the $C_{12}-C_{13}$ bond is twisted by approximately 130° from the



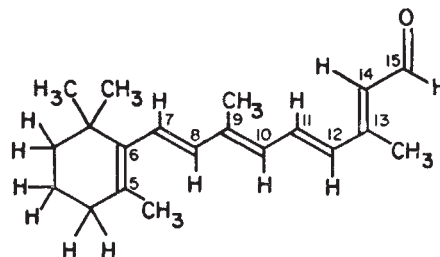
(a) all-trans



(b) 11-cis, 12-s-cis



(c) 11-cis, 12-s-trans



(d) 11-trans, 12-s-cis

I

planar *s-trans* geometry (that is, a distorted *s-cis* conformation, (b)) is slightly more stable than the distorted *s-trans* conformation (60° from planar *s-trans*, (c)) that has been assumed in all previous discussions of 11-*cis* retinal^{1-4,6}. Of course, the quantitative energy differences are not significant and the exact shape of the curve depends on the parameter values (for example, distorted *s-trans* can be slightly more stable than distorted *s-cis*), but the qualitative conclusion that 11-*cis* retinal has a relatively broad and flat minimum is certain to be valid. Thus, the essential difference between the all-*trans* and the hindered 11-*cis* compound, both of which are expected to have 12-*s-trans* conformations with energies similar to 12-*s-trans*, is that in 11-*cis* retinal the *s-trans* and *s-cis* minima are much nearer to 90° (*s-trans*, 60° ; *s-cis*, 130°) and have a much lower barrier between them than in all-*trans* retinal.

The torsion around $C_{11}-C_{12}$, which has been emphasized before^{3,11,12}, is relatively small in 11-*cis* retinal (Table 1).

Definitive experimental information on the geometry of 11-*cis* retinal is not available. A recent nuclear magnetic resonance study¹³ of several isomers, including the 11-*cis* compound, gives qualitative results in agreement with the

calculated potential energy surface, although the data do not distinguish between the *s-cis* and *s-trans* conformation about the $C_{12}-C_{13}$ bond.

It is interesting to consider the spectral consequences of the potential surface shown in Fig. 1. The calculated energy ΔE (eV) and frequency $\tilde{\nu}$ (cm^{-1}) of the lowest $\pi \rightarrow \pi^*$ transition for a series of geometries corresponding to Fig. 1 are listed in columns five and six of Table 1. It is clear that, in the neighbourhood of the minimum energy conformation, there occurs nothing like the complete "break" in conjugation postulated by some workers¹⁴. Values of $\Delta\tilde{\nu}$ (cm^{-1}), the frequency relative to that calculated for the all-*trans* compound, are given in column seven of Table 1. Because "vertical" transition frequencies were calculated for each ground state geometry, the shifts approximate those of the absorption band maxima. The experimental maxima in the room temperature absorption spectra of all-*trans* and 11-*cis* retinal dissolved in hexane are $27,174 \text{ cm}^{-1}$ and $27,397 \text{ cm}^{-1}$, respectively⁴.

Table 1 Energies and Spectra of Retinal as a Function of Geometry

Torsional angles*			E_0 (kcalories)†	ΔE (eV)	$\tilde{\nu}$ (cm^{-1})	$\Delta\tilde{\nu}$ (cm^{-1})‡
$C_{12}-C_{13}$	$C_{10}-C_{11}$	$C_{11}-C_{12}$				
0°	0°	0°	0	3.66	29,520	0
180°	0°	0°	1.77	3.54	28,553	-967
0°	0°	180°	—	3.63	29,279	-241
180°	0°	180°	—	3.52	28,391	-1,129
30°	20°	200°	9.30	3.69	29,763	243
40°	20°	195°	7.75	3.79	30,569	1,049
50°	20°	190°	6.85	3.89	31,376	1,856
60°	10°	190°	6.58	3.95	31,860	2,340
90°	0°	180°	6.90	4.12	33,231	3,711
120°	-15°	175°	5.90	3.93	31,698	2,178
130°	-10°	170°	5.75	3.79	30,569	1,049
140°	-10°	165°	6.15	3.66	29,521	0
150°	-15°	160°	7.0	3.54	28,553	-967

The various geometries are determined as indicated in the text and the legend to Fig. 1; the excitation energies were obtained by a Pariser-Parr-Pople SCF-CI calculation with a modified version of a program from the Quantum Chemistry Program Exchange (Program No. 71.2).

* The listed angles are relative to *trans* as zero and are rounded to 5° because a more precise value is not justified by the calculation; the C_6-C_7 angle is taken to be 135° .

† E_0 is the ground state energy relative to that of planar all-*trans* retinal.

‡ $\Delta\tilde{\nu}$ of the particular conformation minus $\tilde{\nu}$ of all-*trans* retinal.

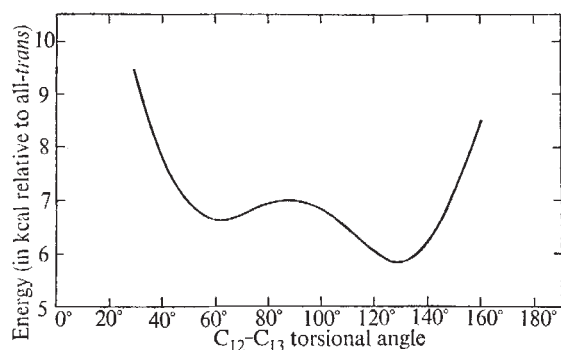


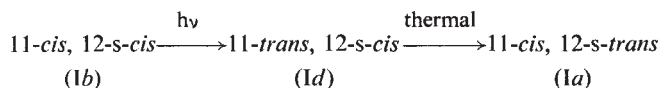
Fig. 1 Potential function for rotation of 11-*cis* retinal about $C_{12}-C_{13}$; $\theta=0^\circ$ corresponds to the *s-trans* linkage. At each point on the curve, the energy $E^\pi + E^{nb}$, where E^π is the Hückel π -electron energy and E^{nb} is a pairwise sum over nonbonded interactions, was minimized with respect to rotation about $C_{10}-C_{11}$ and $C_{12}-C_{13}$; all bond lengths and angles were kept fixed at standard values (C_6-C_7 angle is 135°); nonbonded parameters were from ref. 5, except that a point methyl group was used to simulate free rotation.

What is striking about these values^{4,15,16} is that the 11-*cis* maximum is shifted by only 223 cm⁻¹ relative to the all-*trans* compound. For a molecule like 11-*cis* retinal, in which steric repulsion leads to a ground state geometry that is twisted primarily about single bonds, a shift to significantly shorter wavelengths is expected because the energy of the π^* orbital is raised relative to that of the π orbital. Such high frequency shifts ($\lesssim 2,000$ cm⁻¹), which result in part from variation in vibrational overlap, have been observed in hindered *cis* compounds¹⁵⁻¹⁷. Table 1 shows that at the *s-trans* minimum ($\angle[C_{12}-C_{13}] \approx 60^\circ$) the frequency is displaced by 2,340 cm⁻¹ from that of all-*trans* retinal, while at the *s-cis* minimum ($\angle[C_{12}=C_{13}] \approx 130^\circ$) the shift is only 1,049 cm⁻¹; it is reduced to zero for $\angle[C_{12}-C_{13}] \approx 140^\circ$. To obtain no shift for *s-trans* requires an angle of less than 30°, a highly unstable ground state conformation (Table 1). Comparison of the results for the planar form of 11-*cis* retinal (*s-trans*, $\Delta\tilde{\nu} = -241$ cm⁻¹; *s-cis*, $\Delta\tilde{\nu} = -1,129$ cm⁻¹) demonstrates that the calculated effect is an *s-cis* "redshift" well known in polyene chemistry^{18,19}.

The potential energy curve in Fig. 1 suggests an explanation for the anomalous temperature dependence of the spectrum of 11-*cis* retinal and other hindered polyene isomers^{15,16}. At room temperature the molecule would be expected to undergo transitions from vibrational levels with contributions from a wide range of geometries in the neighbourhood of the *s-trans* as well as the *s-cis* minimum. There would clearly result a broad absorption peak, which could become significantly narrower and more intense at lower temperatures when the molecule is "trapped" in the appropriate minimum energy conformation.

The 11,13-*dicis* isomer of retinal is considerably less stable and has its principal absorption peak at a significantly shorter wavelength than the 11-*cis* isomer²⁰. Both of these results can be understood if 11-*cis* is *s-cis* about C₁₂-C₁₃, and 11,13-*dicis* is a more highly hindered *s-cis* compound or, alternatively, forced into the *s-trans* configuration.

If 11-*cis*, 12-*s-cis* retinal were the chromophore present in the visual system, the initial photoproduct resulting from the isomerization would be a molecule that is *trans* about the C₁₁-C₁₂ double bond but remains *s-cis* about C₁₂-C₁₃, as the C₁₂-C₁₃ bond has more double bond character in the π^* excited state. Because the resulting 11-*trans*, 12-*s-cis* isomer would be essentially planar (without distortion by the lipoprotein), a large redshift due to the *s-cis* conformation is expected; the calculated values are -2,016 cm⁻¹ relative to the distorted 11-*cis*, 12-*s-trans* retinal and -970 cm⁻¹ relative to the planar all-*trans* compound. The ground state planar 11-*trans*, 12-*s-cis* can isomerize thermally to all-*trans* retinal; the calculated barrier is 4 kcalories. The series of reactions



would correspond to the observed changes in the visual pigment spectrum that are associated with the transformations¹



in which the intermediate, prelumi rhodopsin, is strongly redshifted ($-1,680$ cm⁻¹) relative to rhodopsin and lumi rhodopsin, which have similar absorption maxima. That these steps in the rhodopsin cycle are primarily alterations in the chromophore and do not involve significant conformational changes in the lipoprotein complex is in agreement with thermodynamic measurements^{1,2,21,22}.

It is clear that the general features of the torsional potential described in this report must play an important part in the properties of 11-*cis* retinal and other "hindered" *cis* isomers of conjugated systems. The validity of the specific proposals concerning the possible forms of the early intermediates in the visual cycle is far less certain. We have included them primarily as a possible focus for further conformational

studies of these molecules. Details of the calculations, including an interpretation of the shape and temperature dependence of the various absorption bands, will be reported in subsequent publications.

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Role of the Pericorneal Papillary Structure in Renewal of Corneal Epithelium

THE human cornea is covered by a five-layered epithelium. Cells are continually shed from its surface and replaced by division of the basal cells, which has a mean generation time estimated to be about 4 days¹. Because of the papillae in the skin, the relation between the area of the basal cell layer and the surface is about 20:1. Because it must be refractive, there can be no papillae on the cornea, and the relation between the basal cell layer and the surface is accordingly 1:1. This should correspond to higher demands on the generative capacity of the corneal basal cells compared with skin. The epidermal basal cells are in close contact with a well developed capillary network. There are no vessels in the cornea, and so it can be assumed that the supply of its epithelium is poorer. Corneal epithelium, nonetheless, has considerable healing capacity, which is achieved primarily by migration of epithelial cells.

An interesting possibility concerning the renewal of corneal epithelial cells is suggested by study of the transitional zone between cornea and conjunctiva, that is, the limbus corneae. Here the so-called palisades of Vogt are found: fine radial lines about 1 mm long and four per mm of the corneal circumference. Their anatomy and function have given rise to controversy since, in 1859, Manz described limbal epithelial structures in swine, which were thought to be glands. Aurell and Kornerup² concluded that the glands of Manz were rudiments of accessory limbal lachrymal glands. Duke-Elder^{3,4} considered the limbal structures in man to be functionless vestigial traces of the glands of Manz. The limbal palisades consist of subepithelial, richly vascularized papillae (Fig. 1) between which the epithelium projects downwards in radial ridge-like thickenings filling the interstices between the papillae. The palisades are particularly striking in negroes, because the limbal pigment contains melanin, which is seen in thick layer in the epithelial depressions. The radial pigmented lines are sometimes very thin and delicate, and arranged in pairs. This is because the melanin may be concentrated in the basal cell layer, which is directed vertically in relation to the surface along both sides of the papillary crests. It is tempting to suppose that this distinct structure fulfils a purpose.

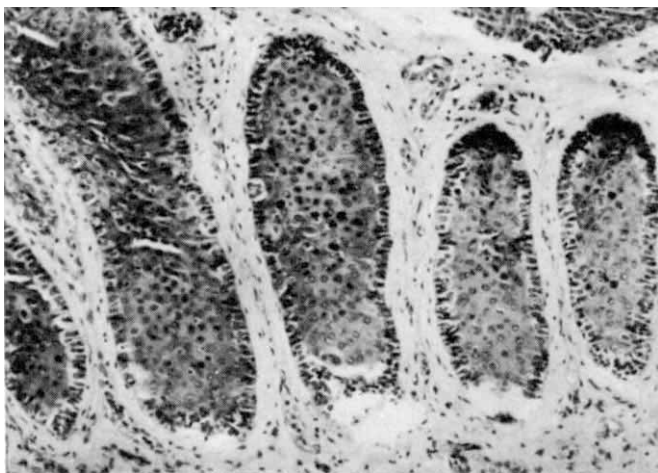


Fig. 1 The papillary limbal structure, the palisades of Vogt. This section, from a negro, is parallel with the limbal surface.

Our theory is that the limbal papillary structure serves as a generative organ for corneal epithelial cells. The generative capacity of the basal cell layer of cornea proper is thought to be insufficient to meet the loss of cells from the surface. To compensate for the deficit, a part of the generative cell population is placed at limbus, where the basal cell layer is large relative to the surface, and is adjacent to a well developed net of capillaries. This would preserve the transparency and refractive properties of the cornea.

The most direct evidence that the limbal structure can produce cells that migrate over the cornea is that if the epithelium is removed from the whole corneal surface, a normal epithelial cover redevelops after some days. The source of these cells must be the epithelial depressions between the limbal papillae.

This is supported by the following experiment. The epithelium was removed in an area adjacent to the pigmented limbal ring in a guinea-pig. Twenty-four hours later the erosion had been covered over with epithelium. This was pigmented over most of the erosion area, and the limbal pigment was lighter in the corresponding area. Five days later the corneal pigmentation had disappeared and the limbal pigmentation was normal. Furthermore, a significantly higher count of colcemid-arrested mitoses was found in the limbal structure of a

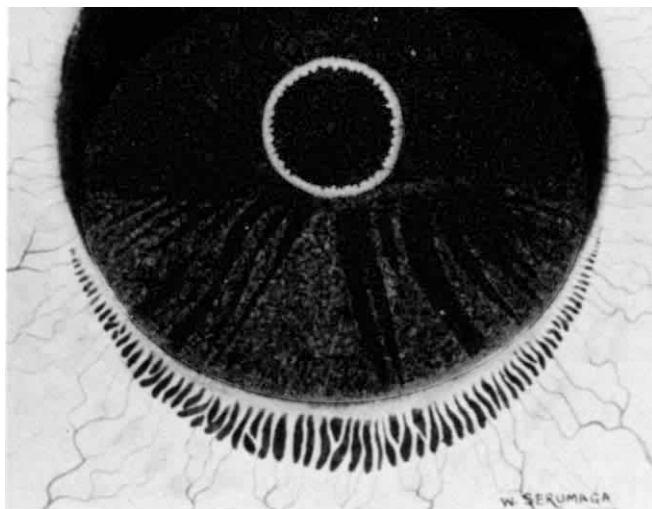


Fig. 2 The limbal and corneal pigmentation in a negro.

guinea-pig's eye in which a central corneal erosion had been made 24 h earlier than in the other eye.

The pattern illustrated in Fig. 2 could be explained by migration from the limbus in normal circumstances. The cells are arranged along lines arcuating from the limbal basal cells towards the cornea. The assumption of a physiological migration of cells is further supported by, and explains, the pigmented lines which curve in over the cornea from the pigmented limbal ring in negro eyes. The melanin is contained in the superficial epithelial cells, whereas the underlying basal cells are not pigmented. The pigmented lines are thought to indicate the direction of migration. These lines are best developed from the inferior limbus, from which they may curve horizontally and come together at a Hudson-Staehli's line. It is thought that this line indicates a border-line of cell migration from the inferior limbus.

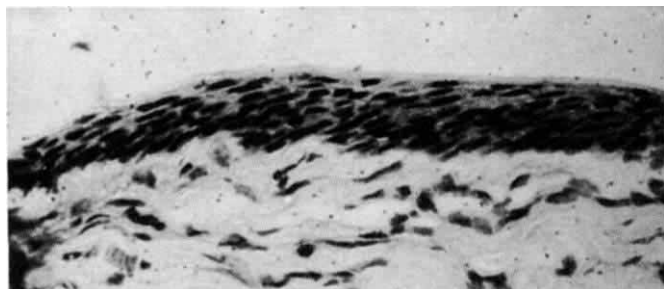


Fig. 3 Radial section through limbus corneae, vertical in relation to the corneal surface (guinea-pig).

A failure in the limbal structure may be the cause of pterygium, a condition in which the corneal surface is invaded by conjunctival tissue. The primary lesion in keratoconus consists of degenerative processes in the basal epithelial cells. These may be caused by a failure in the renewal of the epithelium from the limbal papillary structure.

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Conjecture on the Visual Estimation of Relative Radial Motion

THE ability to estimate accurately the time interval until the juncture of an observer with an object moving with relative radial velocity towards the observer seems to be highly developed in humans and many animals. In many practical situations, of probable importance for survival, it is not the distance of the object from the observer which is of interest, nor is it the velocity of the object, but rather the ratio of the two, which gives the time taken by the object to reach the observer. The importance of this parameter has certainly been renewed in the age of the motor car. The popularity of ball games may be partly due to the exercise of this faculty otherwise dormant in a sedentary era.

I wish to show here that there is sufficient information available on the monocular retina to allow the observer to estimate the time of juncture with the moving object without the need for absolute knowledge of the distance of the object, its size or its velocity.

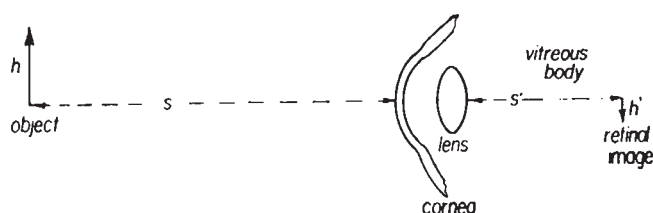


Fig. 1 Optical system of the eye of the observer and an object moving with uniform radial velocity towards the observer (not to scale).

Fig. 1 shows schematically an optical system representing the eye of the observer and an object of size h at a distance S from the observer. If v is the relative uniform velocity of the object towards the observer then the time interval until juncture is given by

$$t = \frac{S}{v} \quad (1)$$

For paraxial rays Lagrange's law gives for the image size h' on the retina

$$h' = \frac{h}{S} \frac{S'}{n'} \quad (2)$$

where S' is the distance of the retina from the lens and n' the index of refraction of the vitreous humour.

Differentiating equation (2) with respect to time gives

$$\frac{dh'}{dt} = -\frac{dS}{dt} \frac{hS'}{S^2 n'} = v \frac{hS'}{S^2 n'} \quad (3)$$

because S' may be assumed constant.

Dividing equation (2) by equation (3) gives

$$\frac{h'}{\frac{dh'}{dt}} = \frac{S}{v} = t \quad (4)$$

that is, the time interval of interest.

Thus a knowledge of the instantaneous image size and its time derivative is sufficient to determine, with monocular vision alone, the juncture interval without requiring absolute knowledge of S , v or even h .

The verification of the conjecture that the visual system is sufficiently adept to estimate the time interval to juncture from the limited but sufficient retinal information is an interesting experimental problem.

Commenting on this conjecture, Professor R. L. Gregory (private communication) has remarked: "Visual size is not, of course, merely a matter of retinal size and it is not very clear how the information of the retinal size is retained after 'constancy scaling'. This itself is an interesting question and I would like to know the answer."

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Changes in Adrenal Enzymes synthesizing Catecholamines in Attack Behaviour evoked by Hypothalamic Stimulation in the Cat

IN the cat, electrical stimulation^{1,2} or selective lesions of the brain³ can evoke an affected display of anger, called sham rage³. This emotional display is often coupled with directed prey killing or attack behaviour². Associated with this is a widespread activation of the sympathetic nervous system and a release of the catecholamines, noradrenaline and adrenaline, from the adrenal gland^{4,5}. It was recently demonstrated that, when prolonged, increased neural release of adrenal catecholamines is associated with increased activity of tyrosine hydroxylase^{6,7}, the enzyme of the rate-limiting step in catecholamine biosynthesis⁸. The increase in enzyme activity is presumably the result of production of new enzyme^{6,9}. We have sought to determine whether the induction of attack behaviour in the cat by electrical stimulation of the hypothalamus, if sustained over several days, can lead to similar changes in adrenal tyrosine hydroxylase and also the adrenal enzyme phenylethanolamine-N-methyl transferase (PNMT) which converts nor-epinephrine to epinephrine.

In a preliminary operation, adult cats were placed under halothane anaesthesia and electrode guides were stereotactically placed through drill holes in the calvarium, over sites in the posterior hypothalamus from which attack behaviour can be evoked². Several days later the animals were placed in an observation cage with an anaesthetized rat and an insulated monopolar electrode with a 0.5 mm bare tip was lowered and fixed into the locus at which rat-killing behaviour could be evoked by electrical stimulation. The anode was a screw embedded in the skull. In controls, the electrode was placed in immediately adjacent hypothalamic regions from which some motor activity but not rage or prey-killing could be elicited. Animals were electrically stimulated from a constant current stimulator for 90 min in the morning and in the afternoon for 3 consecutive days. The stimulus programme consisted of 2 min trains of square wave pulses (0.5 ms duration, 0.5–2.0 mA, 70 c.p.s.) each followed by a 3 min rest. After the last stimulation session, the animals were lightly anaesthetized with

Table 1 Enzyme Activity in Adrenal Gland after Brain Stimulation

	Tyrosine hydroxylase*	PNMT*
Control (n)	93.8 ± 9.6 (13)	14.1 ± 1.7 (13)
3 day stimulation, no attack (n)	157 ± 34.3 (10) NS	13.7 ± 2.0 (10) NS
3 day stimulation, attack (n)	412 ± 44.6 † (10)	30.4 ± 2.1 † (12)

* Activity expressed by nmol of product/100 mg/20 min ± s.e.m.

† Difference from control significant ($P < 0.001$).

NS, Difference from control not significant ($P > 0.05$).

Table 2 Effects of Unilateral Adrenal Denervation on Enzyme Activity of Adrenal Gland after Brain Stimulation

	Tyrosine hydroxylase*		PNMT*	
	R	L (denervated)	R	L (denervated)
Control	84 ± 9.0	105 ± 17	11.7 ± 13	10.3 ± 0.7
(n)	(7)	(6)	(7)	(6)
3 day stimulation, no attack	179 ± 50	112 ± 35	14.7 ± 3.9	9.1 ± 3.4
(n)	(3)	(3)	(3)	(3)
Change from control	NS	NS	NS	NS
3 day stimulation, attack	257 ± 18	112 ± 12 †	18.7 ± 2.1	11.8 ± 1.6 ‡
(n)	(6)	(6)	(6)	(6)
Change from control	<0.001	NS	<0.02	NS

* Activity expressed as nmol of product/100 mg/20 min ± s.e.m.

† Difference from right gland significant ($P < 0.001$).

‡ Difference from right gland significant ($P < 0.02$).

NS, Not significant.

chloroform, killed by decapitation, and the adrenal glands removed and frozen in dry ice.

The adrenal glands were weighed, homogenized in 4 volumes of 0.25 M sucrose and centrifuged to remove debris. The supernatants were recentrifuged at 100,000g to spin out the microsomal fraction and then dialysed. Enzyme activity¹⁰ was assayed by end-product inhibition. The pellet from high speed centrifugation of the adrenal gland was re-homogenized in 0.02 M K_2PO_4 buffer (pH 6.5) and aliquots were taken to assay tyrosine hydroxylase by the method of Nagatsu *et al.*¹⁰ and PNMT by the method of Axelrod¹¹. No differences in enzyme activities were found between the right and left adrenal glands.

Changes in the activity of adrenal tyrosine hydroxylase and PNMT can be seen in Table 1. After 3 days of stimulation producing attack behaviour the tyrosine hydroxylase activity increased to four times the original value and PNMT activity doubled. In stimulated controls there was no change in enzyme activity.

To determine whether the increased activity of adrenal tyrosine hydroxylase and PNMT depended on the neural innervation of the adrenal gland, the left adrenal gland was denervated. Changes in enzyme activity in innervated and denervated adrenals were measured in unstimulated controls, stimulated animals with attack behaviour and stimulated animals without attack behaviour (Table 2). Brain stimulation which produced attack behaviour tripled the activity of tyrosine hydroxylase and almost doubled the activity of PNMT in the innervated gland. Electrical stimulation producing alertness or movement but not attack did not cause significant changes in enzyme activity. In the denervated gland, enzyme activity did not increase. Thus the increase in activity of both adrenal enzymes after hypothalamic stimulation depends on intact innervation to the adrenal medulla and therefore probably involves efferent nerve impulses.

This study demonstrates that intermittent electrical stimulation of the hypothalamus during 3 days can lead to increased activity of tyrosine hydroxylase and PNMT in the adrenal gland. Moreover, the changes in enzyme activity seem to be behaviourally specific, for they do not occur when hypothalamic stimulation failed to evoke attack behaviour. The failure of enzyme activity to increase in the denervated adrenal gland indicates that the increase in enzyme activity depends on nerve impulses. In the adrenal gland tyrosine hydroxylase has been shown to be increased by nerve impulse activity in immobilization stress¹² and presumably after reserpine^{7,13}. While increased activity of PNMT occurs after reserpine treatment, presumably through a neurogenic mechanism¹³, the work described here provides the first direct evidence for a neural participation in the regulation of this important enzyme. Because nerve impulses are also necessary for the release of adrenal catecholamines in sham rage^{4,5} it is possible that the amines themselves play a part in regulating the rate of enzyme synthesis.

Activation of the sympathetic nervous system and enhanced secretion of adrenal catecholamines are a common denominator in behaviour in which animals are prepared for fight or flight. This view, proposed by Cannon¹⁴, emphasizes the utility of catecholamine release for the immediate physiological adaptation of visceral and metabolic activity to the emotional arousal. The present study adds another dimension to this concept. It suggests that, when sustained, behaviour characterized by sympathetic and adrenomedullary hyperactivity can lead to changes in enzymes involved in the synthesis of the transmitters themselves. The changes seem to increase the availability of catecholamines at receptors by increasing the activity of critical enzymatic steps essential for synthesis. The consequences of these changes for long range behavioural and visceral control, however, remain to be elucidated.

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Duration of *in vivo* Effects of L-Asparaginase on Experimental Metastasis

L-ASPARAGINASE has been used to treat various neoplasms in man and animals¹⁻⁴, and was at first believed to act only on malignant cells which are dependent on asparagine. Clinical investigations, however, indicated that L-asparaginase could itself be antigenic⁵ and have serious side effects. Moreover, L-asparaginase has been found to lead to suppression of phytohaemagglutinin-induced blastogenesis of human lymphocytes⁶⁻⁸. Depression of the immune response to sheep red blood cells in mice treated with the enzyme has been reported⁹. Inhibition of the graft versus host reaction in rats and mice¹⁰ as well as reduction of the immune reactivity to an allografted tumour¹¹ have also been observed.

The amounts of L-asparaginase necessary to produce regression of sensitive tumours have been worked out, but the frequency of administration required for optimal *in vivo* effects is not known. We report here the effects of L-asparaginase on the incidence of experimental metastasis and describe an assay to determine the duration of *in vivo* effects of a single dose of the enzyme.

B16 melanoma adapted to grow in tissue culture was used in C57BL/6J mice. *In vitro* cytotoxicity studies with various concentrations of L-asparaginase (1–50 IU/ml. media) revealed no inhibition of growth. Five groups of mice (12–14 weeks old) were injected intraperitoneally with 5,000 IU/kg of L-asparaginase (Merck, Sharp, and Dohme) each day; control groups were injected with saline. The start of treatment ranged from 3 days before to 3 days after intravenous inoculation of 50,000 B16 melanoma cells. Treatments were carried out daily until the seventh day after injection of tumour cells. Mice were killed on the fourteenth day and their lungs were removed. Pulmonary metastases were counted under a dissecting microscope. Student's *t* test was used in all evaluations of differences between means of each treatment group and its matched control. The results (Table 1) demonstrated that there were significantly more lung metastases ($P < 0.001$) in the mice treated with L-asparaginase before or on the day of tumour inoculation, compared with controls. No differences in the incidence of metastases were demonstrable between mice treated with L-asparaginase after tumour cell injection and controls.

Table 1 Incidence of Lung Metastases in Mice injected Intravenously with Melanoma Cells and treated with L-Asparaginase or Saline

Start of treatment	No. of lung metastases *	
	L-Asparaginase	Saline (control)
3 days before tumour †	176 ± 14	68 ± 9
2 days before tumour †	180 ± 17	67 ± 7
1 day before tumour †	182 ± 14	70 ± 11
Same day as tumour †	108 ± 11	62 ± 9
1 day after tumour ‡	80 ± 9	72 ± 14
2 days after tumour ‡	68 ± 6	67 ± 7
3 days after tumour ‡	69 ± 7	64 ± 6

* Mean number of lung nodules in eight animals (per group).

† Lung metastases in L-asparaginase and saline-treated animals differed significantly ($P < 0.001$).

‡ No statistical differences in the number of lung metastases were demonstrated.

We then determined the duration of the effect of a single dose of L-asparaginase on the incidence of experimental metastasis. C57 mice, divided into six treatment and control groups, received a single intraperitoneal injection of 5,000 IU/kg of L-asparaginase or of saline. Injections were given at different times, from 7 days before, to the same day as the intravenous injection of 60,000 B16 melanoma cells. Animals were killed 14 days later, and the lung metastases were counted. The results (Table 2) showed that there were significantly more lung metastases ($P < 0.001$) in mice treated once with L-asparaginase

Table 2 Duration of *in vivo* Effects of a Single Dose of L-Asparaginase on the Incidence of Experimental Metastasis

Single dose day of treatment	No. of lung metastases *	
	L-Asparaginase	Saline (control)
7 days before tumour †	55 ± 5	56 ± 5
5 days before tumour †	53 ± 6	60 ± 9
3 days before tumour †	50 ± 5	58 ± 6
2 days before tumour †	83 ± 7	52 ± 7
1 day before tumour ‡	154 ± 13	59 ± 5
Same day as tumour ‡	135 ± 14	53 ± 6

* Mean number of lung nodules in seven animals (per group).

† Comparison of L-asparaginase and saline treated animals demonstrated no difference in the number of lung metastases.

‡ The number of lung metastases in L-asparaginase and saline treated controls differed significantly ($P < 0.001$).

either on the same day, or 1 or 2 days before tumour cell injection, than in the controls. On the other hand, in animals treated with L-asparaginase 3 or more days before tumour cell injection there was no increase in the number of lung metastases.

Thus we can conclude that L-asparaginase increases the incidence of pulmonary metastases, and that this increase may be due to host immunosuppression. Furthermore, in our system the duration of this effect after a single dose has been found to be about 48 h, so that administration of L-asparaginase to achieve immunosuppression might only be necessary every 2 or more days.

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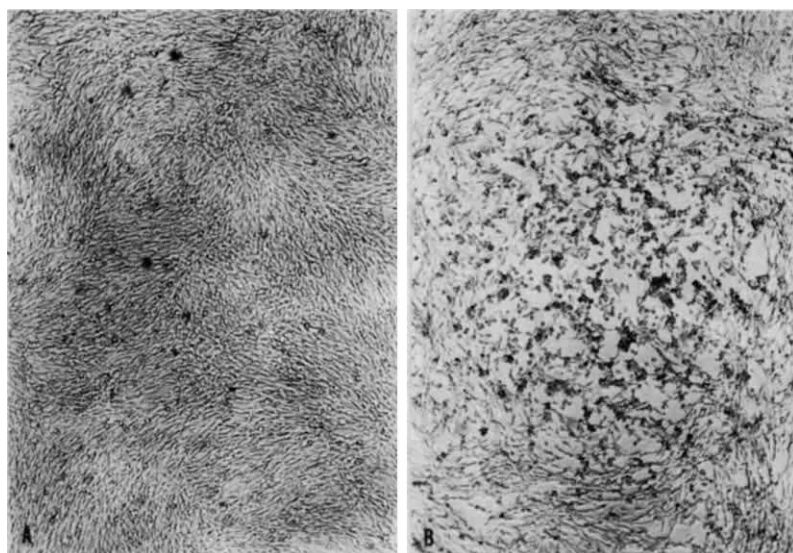
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Rapid Cell Culture Assay Technique for Murine Leukaemia Viruses

INFECTION of susceptible mouse cells in culture with murine leukaemia viruses (MLV) does not cause any observable change in cellular morphology, even though continuous virus replication in these cells can often be demonstrated. Complement-fixation¹ and fluorescent antibody² techniques as well as interference³ or potentiation⁴ of focus formation by "defective" murine sarcoma viruses have all been used successfully to detect and to quantitate *in vitro* infection of mouse cell cultures with MLV. These techniques, however, are less than ideal because they involve special reagents and lengthy incubation, or because they are relatively insensitive. Klement *et al.*⁵ have shown that the XC cell line⁶, derived from a rat

Fig. 1 A, Control S+L- mouse cells. B, Lytic focus with characteristic clusters of round cells appearing in S+L- cells 5 days after superinfection with MLV. Unstained; $\times 48$.



tumour induced by the Prague strain of Rous sarcoma virus, undergoes syncytium formation when present in mixed cultures together with MLV-infected mouse cells. This phenomenon of mixed culture cytopathogenicity has been used to develop a plaque assay for murine leukaemia viruses in mouse cell cultures (unpublished observations of W. P. Rowe *et al.*).

During the course of our experiments, designed to study the interrelationships between "defective" murine sarcoma viruses (MSV) and MLV, we were able to isolate transformed 3T3 mouse cells which contained the MSV genome in the absence of detectable MLV^{7,8}. Normal 3T3 cells were infected with dilutions of MSV and immediately plated as suspension cultures in media containing 0.3% agar. Colonies of transformed cells, proportional to the concentration of MSV used for infection, first appeared after approximately 2 weeks and increased steadily in size. Several colonies were isolated from the agar suspension plates and grown as monolayer cultures. Some of these colonies gave rise to viable cell lines which continuously released MSV into the culture medium, while other colonies yielded monolayer cultures containing MSV-transformed cells but from which no focus-forming MSV could be recovered. These latter cells, termed "sarcoma positive leukaemia negative" (S+L-), did not release detectable quantities of MSV unless superinfected with any of several strains of MLV, and seemed to contain the MSV genome in the absence of replicating leukaemia virus. One of the S+L- cell lines, in addition to releasing MSV after superinfection with MLV, responded with the formation of MSV-type foci proportional to the concentration of MLV used for superinfection⁸. The response of this line of S+L- cells to superinfection with MLV can be used as the basis for a rapid and sensitive assay technique, the details of which are described in this report.

S+L- cells were obtained by two successive isolations of individual colonies from microplates (Falcon Plastics, Los Angeles) inoculated with the "C-116" line, a mixture of

S+L- cells and apparently normal cells⁸. This procedure increased the proportion of S+L- cells in the mixed population to approximately 40% from the 7% in the original C-116 cell line, and a corresponding increase in sensitivity to focus induction was noted.

For leukaemia virus focal assays, S+L- cells were plated in 60 mm plastic Petri dishes at a concentration of 10^5 cells per dish and infected the following day with dilutions of MLV. Five days after infection, foci could be easily seen by microscopy. These foci appeared as lytic areas in the confluent cell sheet characterized by the presence of grape-like clusters of round cells (Fig. 1). Alternatively, infected plates could be stained with May-Grünwald and Giemsa, and the foci counted by microscopy (Fig. 2). The numbers of foci produced by a variety of MLV preparations studied to date were directly proportional to the concentration of virus (Table 1). Friend, Moloney and Rauscher murine leukaemia viruses have all been used to produce foci by this assay technique. Standard preparations of these viruses contained more than 10^6 infectious units per ml. as calculated from the numbers of detectable foci induced in S+L- cells. Radiation leukaemia virus (RadLV)⁹ also induced similar cellular changes in S+L- cells, although the foci were distinctly smaller in size and contained few round cells, suggesting that this virus multiplies poorly or not at all in the target cells. Active MSV could be detected in culture fluids from all S+L- assay plates which contained MLV-induced foci.

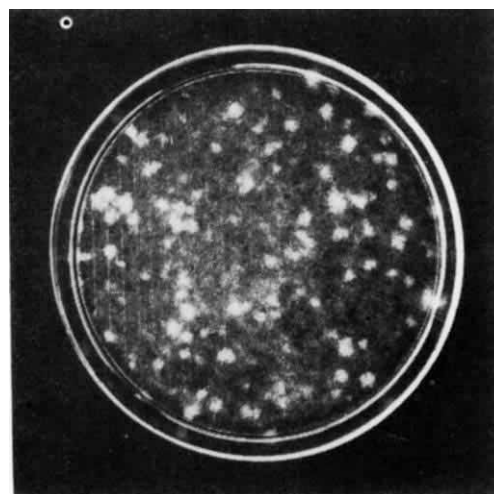


Fig. 2. Petri dish (60 mm) containing approximately 80 foci, 5 days after superinfection of S+L- cells with diluted MLV. May-Grünwald and Giemsa stain; oblique lighting.

Table 1 Focus Induction in S+L- Cells by Murine Leukaemia Virus (IC Isolate)

Virus dilution (0.2 ml./dish)	Focus counts	Average No. foci/dish	Titre estimate *
$10^{-3.1}$	Confluent	Confluent	—
$10^{-3.6}$	Confluent	Confluent	—
$10^{-4.1}$	41, 64, 50, 68	55.8	$10^{6.55}$
$10^{-4.6}$	12, 13, 26, 18	17.3	$10^{6.54}$
$10^{-5.1}$	8, 5, 6, 6	6.3	$10^{6.60}$
Control	0, 0, 0, 0	0	—

* Estimate of focus-inducing units/ml. in original MLV preparation based on numbers of foci at each virus dilution.

Antiserum to the IC isolate of MLV¹⁰, prepared in BALB/c mice by University Laboratories, Highland Park, New Jersey, was highly active in neutralization tests using the S+L- cell assay system. In a two dimensional reaction in which the quantities of both IC virus and its specific antiserum were varied, the proportion of virus neutralized by a given dilution of serum seemed to be independent of the number of focus-inducing units of leukaemia virus (Table 2).

Table 2 Neutralization of Murine Leukaemia Virus (IC Isolate) by Homologous Mouse Antiserum

Antiserum dilution (final)	Focus-inducing units of IC virus added:						
	3,160	1,000	316	100	31.6	10	0
1:20	35*	7	2	1	—	—	—
1:40	140	29.5	15	2.5	—	—	—
1:80	C†	112.5	45	14	—	—	—
1:160	C	C	142	33.5	11	—	—
1:320	C	C	C	65.5	17.5	—	—
Control	C	C	C	99.5	29.5	10	0

* Average number of foci in two Petri dishes.

† Confluent.

The sensitivity of focus induction in S+L- cells as a measure of MLV activity was compared with that of several other *in vitro* assay techniques. Dilution end point estimates of the amount of replicating virus present in a preparation of IC leukaemia virus were determined in normal 3T3FL⁸ mouse cells by measuring induction of interference to MSV or by recovery of "helper" activity for MSV. Quantitatively, these assays gave results which were in close agreement with titres of the same leukaemia virus preparation based on focus assays in S+L- cells. In addition, a preparation of Rauscher leukaemia virus previously assayed in the XC plaque test by Dr Willie Turner of the National Cancer Institute was found to have an identical titre when assayed by focus induction in S+L- cells.

The close correlation between the number of focus-inducing units of MLV in a leukaemia virus preparation and the end point for virus replication measured by several different methods indicates that MLV replication is necessary for focus induction in S+L- cells. Leukaemia viruses such as RadLV, which replicate poorly or not at all in mouse cell cultures, may still be detected by their ability to rescue transforming MSV from S+L- cells, a possibility which is currently under investigation.

Cell lines containing mixtures of S+L- and normal cells develop MLV-induced foci which are easier to enumerate than do lines containing only S+L- cells, since the latter do not readily form confluent monolayers. The quantitative effect of the presence of normal cells together with S+L- cells in the assay system was determined by infecting a mixed cell line with terminal MLV dilutions. Cells from assay plates which did not contain overt foci were passed blindly for 17 days and then tested for MSV production. The MLV titre calculated directly from the numbers of foci induced in the mixed cell line differed only two-fold from the end point dilution estimate of MLV activity based on recovery of MSV from the same cells. These results indicate that focus assays in mixed cell lines detect all, or nearly all, of the MLV capable of replicating in these cells. Passage of two different mixed cell lines for periods of up to 3 months in two different laboratories has not resulted in any noticeable quantitative change in focus formation by MLV, as might be expected if there were a marked change in the proportion of S+L- cells in the population.

In summary, focus induction by MLV in mouse cell lines containing relatively high proportions of S+L- cells is an exceedingly simple and convenient method for the detection

and quantitation of murine leukaemia viruses and is comparable in sensitivity to other *in vitro* methods currently in use.

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Participation of θ -Bearing Cell in an *in vitro* Assay of Transplantation Immunity

For several humoral immune reactions, cellular interaction between thymus processed and non-thymus processed lymphocytes is required¹⁻⁴. Lymphoid interaction has also been demonstrated in allograft immunity⁵, in the graft versus host reaction⁶⁻⁸ and in an *in vitro* heterograft reaction system⁹. Both in humoral^{2-4,10} and in transplantation immunity⁹, the cell which initiates the response—the antigen reactive cell—is derived from the thymus. The nature of the effector cell, however, is known only in the case of certain humoral immune reactions, in which it has been demonstrated that antibody is secreted by the non-thymus processed, bone marrow-derived cell^{11,12}. The origin of the effector cell in transplantation reactions is unknown.

We have used anti- θ AKR serum¹³ to determine whether the effector function (*in vitro* destruction of target cells) of immune AKR lymphocytes is dependent on cells of thymic origin. Such serum has been shown to eliminate selectively thymus derived cells from a heterogeneous lymphoid cell population¹⁴.

Young AKR mice were grafted with C57Bl/6 skin and 11 days later their draining lymph nodes were collected. Suspensions of the sensitized lymphoid cells were prepared and treated with various dilutions of C3H anti- θ AKR serum or normal C3H serum, in the presence or absence of complement. After treatment lymph node cells were plated on C57Bl/6 target fibroblasts prelabelled with ⁵¹Cr for the assay of immune lysis^{9,15}. Untreated, sensitized and unsensitized AKR lymph node cells were also assayed.

The results of the *in vitro* graft reaction are presented in Table 1. An inhibition of target cell lysis of approximately 20% was observed when sensitized lymph node cells were incubated with normal serum and complement, or with anti- θ serum without complement. This decrease in lytic activity (compared with untreated, sensitized lymph node cells) presumably reflects some damage to the cells caused by

Table 1 Effect of Anti- θ AKR Serum on the Ability of Sensitized AKR Lymphocytes to lyse C57Bl/6 Fibroblasts *in vitro*

Experiment No.	Dose and type of lymphocytes	Treatment	c.p.m. * released	c.p.m. * total	Net % [†] ⁵¹ Cr released	% inhibition
1	Spontaneous release ‡		2,482	9,092	—	—
	5 × 10 ⁶	None	3,498	9,058	15.4 ± 2.2	0.0
	sensitized cells	0.05 ml. a- θ	3,251	8,778	12.2 ± 0.2	20.8
		0.05 ml. a- θ + C'	2,583	9,445	1.4 ± 0.7	90.9
		0.10 ml. a- θ + C'	2,560	9,523	1.3 ± 0.6	91.6
2	5 × 10 ⁶	None	3,670	9,402	17.2 ± 1.3	0.0
	sensitized cells	0.05 ml. normal serum + C'	3,426	9,579	13.3 ± 0.8	22.6
		0.05 ml. a- θ + C'	2,615	8,940	1.9 ± 0.9	89.0
		0.10 ml. a- θ + C'	2,549	9,037	1.0 ± 0.5	94.2
3	Spontaneous release ‡		2,607	9,079	—	—
	10 × 10 ⁶ non-sensitized	None	2,774	8,736	2.7 ± 2.5	—
	10 × 10 ⁶	None	3,760	7,536	23.3 ± 1.9	0.0
	sensitized cells	0.05 ml. normal serum + C'	3,227	7,250	17.0 ± 0.9	27.0
		0.005 ml. a- θ + C'	3,534	7,838	17.7 ± 1.4	24.0
		0.01 ml. a- θ + C'	3,850	8,755	20.2 ± 1.1	13.4
		0.02 ml. a- θ + C'	3,223	7,878	11.3 ± 4.7	51.5
		0.05 ml. a- θ + C'	2,501	8,492	0.8 ± 2.0	96.6
		0.10 ml. a- θ + C'	2,329	8,139	0.0	100.0

Female AKR/J mice, 2.5 months old, were grafted with C57Bl/6 skin. Eleven days later the draining lymph nodes were collected and a cell suspension prepared in Eagle's medium plus horse serum (20%). Lymphoid cells were preincubated with varying amounts of anti- θ serum or normal C3H serum, in the presence or absence of Difco guinea-pig complement (C'). After 1 h lymphoid cells were washed and 5 or 10 × 10⁶ cells were plated on fibroblast monolayers labelled with ⁵¹Cr (0.7–1.0 × 10⁶ fibroblast/plate). ⁵¹Cr released was determined after 48 h^{9,15}.

* Mean value of two to seven replicates.

† Net % ⁵¹Cr released was calculated according to Brunner *et al.*¹⁶

‡ Target monolayers labelled with ⁵¹Cr were incubated for 48 h with Eagle's medium and horse serum only, to determine spontaneous release of ⁵¹Cr.

the additional handling (centrifugation, incubation, washing and so on). On the other hand, sensitized cells pretreated with 0.05–0.10 ml. of anti- θ serum per culture plus complement lost essentially all their lytic activity and this effect is antibody-dose dependent (experiment 3, Table 1). Unsensitized AKR lymphocytes did not produce any lytic effect, indicating that it is unlikely that during the assay period any additional sensitization occurred.

We (unpublished observations) and Raff¹⁴ have observed that anti- θ immune serum eliminates 85–90% of thymus lymphocytes, but only 50% of lymph node and 30% of spleen lymphocytes. In cultures containing the highest concentration of anti- θ serum, and in which lytic activity was essentially completely abolished, a considerable number of lymphoid cells were still viable at the end of the assay period. These might be cells which do not bear the θ antigen marker.

Our results suggest that the *in vitro* lytic activity of sensitized lymph node cells depends on the function of cells bearing the θ antigen. These findings exclude the possibility that the lytic function is performed solely by bone marrow-derived or other cells not bearing the θ marker, but they do not demonstrate in an exclusive way that the thymus-derived cell is the only cell causing the cytolytic effect. The fact that we have only a thymus-specific reagent (anti- θ), and that at present we do not have lymphotoxic immune sera of other specificities, leaves open another possible interpretation, besides an exclusive effector role of thymus derived cells. The cytolytic damage could be caused by cells of more than one type—thymus and some other cell type, such as bone marrow-derived—wherein one cell would be involved in causing the actual target cell destruction and the other would fulfil some auxiliary function.

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Induction of Lactogenesis and Abortion by Prostaglandin $F_{2\alpha}$ in Pregnant Rats

THE withdrawal of ovarian progesterone at the end of pregnancy seems to be the essential step in the initiation of lactation in pregnant rats¹⁻⁵. Although there is a decrease of plasma progesterone concentration before parturition^{6,7}, the mechanisms involved in the regression of the corpus luteum at parturition are unknown. It is known⁸⁻¹⁰ that the uterus is concerned with the regression of the corpus luteum in the rat and the uterine luteolytic seems to involve a substance transported in the blood¹⁰. The discovery of prostaglandins in menstrual fluid and human endometrium^{11,12} and the luteolytic action of prostaglandin F_2 ($PGF_{2\alpha}$) demonstrated in pseudopregnant rats¹³ and normal guinea-pig¹⁴ indicate a possible participation of prostaglandin at the end of pregnancy. The high concentration of $PGF_{2\alpha}$ in the amniotic fluid during labour¹⁵ gives support to this hypothesis.

I have investigated the effect of $PGF_{2\alpha}$ in eight pregnant rats of the Instituto strain, housed in individual cages. They were injected intraperitoneally with 1.2 mg of $PGF_{2\alpha}$ in four doses of 0.3 mg each, every 4 h on day 17 (two rats) and day 18 (six rats) of pregnancy. $PGF_{2\alpha}$ was prepared as recommended by the makers (Upjohn). A control group of ten rats was injected with four doses of normal saline on day 17 of pregnancy. The following day, 12 and 17 h after the administration of the last dose of saline or prostaglandin, an oxytocin test⁴ was performed to determine the onset of lactogenesis.

All animals were checked several times a day for signs of abortion. After parturition, maternal behaviour was watched in each treated rat.

None of the control rats gave a positive response to the oxytocin test. In this strain lactogenesis takes place 12 h before parturition on day 22 (ref. 4). All control rats delivered normal foetuses at term. But when the oxytocin test was applied to the eight treated rats 15 h after the last injection of $PGF_{2\alpha}$ visible milk appeared. No rats gave a positive response in the first test. It is interesting that after the last dose of $PGF_{2\alpha}$, rats adopted the typical posture of parturition for at least 1 h; contractions were also observed through the abdominal wall. Four rats were injected with 100 mU of oxytocin 30 min after the last dose of prostaglandin, to see whether abortion could be induced. None aborted, but blood was seen in the vagina of some rats. On day 20 of pregnancy all rats treated with $PGF_{2\alpha}$ delivered small foetuses, some of them alive. Maternal behaviour was studied by giving a foster litter to each rat on the day after parturition. Seven rats showed normal maternal behaviour but only two were able to feed the young.

These results show clearly that $PGF_{2\alpha}$ can induce lactogenesis and advance parturition when injected into pregnant rats. According to previous knowledge^{13,14} $PGF_{2\alpha}$ may have a luteolytic effect in pregnant rats and may be responsible for the decrease in progesterone at the end of pregnancy. There is no evidence about the mode of action of $PGF_{2\alpha}$ in pregnant rats. The suggestion of a venoconstrictor action affecting the life span of the corpus luteum¹³ has been shown to be incompatible with the normal development of the rest of the ovary after treatment with prostaglandin¹⁴. Further work is needed to clarify the function of $PGF_{2\alpha}$ as the luteolytic factor before parturition.

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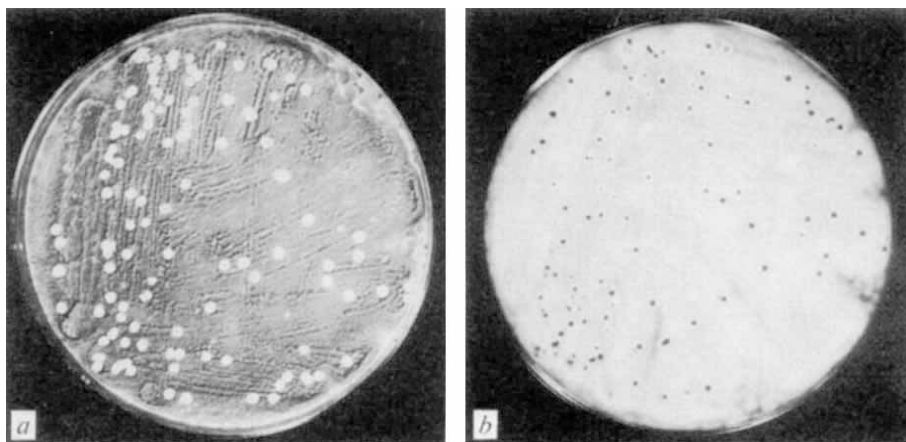
Production of Lytic Plaques of Viral Origin in *Penicillium*

THE presence of virus particles in fungi is now established on the basis of observations in *Agaricus (Psalliota) bisporus* and in *Penicillium stoloniferum*^{2,3} and *P. chrysogenum*⁴. Viruses in *A. bisporus* cause several malformations of the fruiting body⁵ and some morphological variations of the colony in *P. stoloniferum*³. Small patches of white aerial mycelium have frequently been observed on the surface of fungi and we have confirmed this for *P. citrinum* and *P. variable* grown on potato glucose agar at 24° C. When these organisms are grown on 18% lactose, 1% peptone, 2% agar, distilled water (pH 6.5) (medium A) at 24° C, lytic plaques are observed on the reverse of the patches of white aerial mycelium (Fig. 1a, b), which are morphologically similar to those produced by bacteriophages in bacteria and in streptomycetes. The mycelium taken from the centre of the lytic area consists of swollen hyphae, wholly lysed or with very little cytoplasm. Observation with the electron microscope, after fixation with phosphotungstate (PTA) at pH 7, has shown that the hyphae yield a large amount of virus particles (2 to 100 per field) as previously observed¹⁻⁴. The particles have a hexagonal shape, with no tail and a diameter of 400–500 Å.

We tried to determine whether the presence of virus could cause some modification of the normal morphology of the two species under examination. Two culture types were isolated in medium A; type 1 was obtained from the mycelium taken from the centre of a lytic plaque; type 2 was obtained from mycelium taken from the white patches present on the colony surface. Type 1 gave moist, yeast-like colonies without aerial mycelium, and which were sterile; type 2 gave fluffy round colonies, with abundant aerial mycelium; they also were sterile. Only the type 2 colonies contained a large amount of virus particles (15–30 per field) like those observed in the lytic plaques. The virus particles were not found in the type 1 colonies, nor in the normal mycelium of the two species of *Penicillium* under examination. Type 2 colonies, grown at 30°–32° C, reverted to normal—that is conidia were formed again. At these temperatures therefore it seemed that the fungus recovered from the virus infection, as observed by others^{1,3} for subcultures at 24° C.

To reproduce the lytic plaques, we broke each plaque with a cotton swab, took out the infected mycelium and the conidia of the surrounding healthy mycelium, and smeared this evenly on 20 ml. of medium A in 10 cm Petri dishes (the thickness of the agar seemed to be critical). After 5–10 days at 24° C a

Fig. 1 *a*, *P. variable*, upper surface of the colony with several patches of white aerial mycelium. *b*, Reverse side of the colony of *P. variable* showing the presence of several lytic plaques which coincide with the white patches.



large number of lytic plaques of various shapes and sizes were observed, this being related to the type of carbon source and to its concentration. Using medium A, it was found that the optimal carbon source was given by 10% sucrose or 18% lactose. The lytic plaques are inhibited by the addition to medium A of the sodium salt of mycophenolic acid at the minimal concentration of 1 $\mu\text{g/ml}$. Attempts to transmit the infection from infected to healthy strains have proved unsuccessful.

It is possible to draw the following conclusions. Two species of *Penicillium* show lytic plaques containing some viruses, similar to those produced by bacteriophages. Patches of white aerial mycelium seen at the surface of the colonies of the two species of *Penicillium* result from a viral infection that in turn brings about a marked morphological modification of the fungus. The yeast-like colonies (type 1) do not show any virus particles. Their stability, even when grown at 30°–32° C, suggests that in them the virus is linked to the chromosomes, that is, it is in temperate form. Mycophenolic acid inhibits the appearance of lytic plaques and therefore it seems to have an antiviral activity in fungi similar to that shown against some animal viruses^{6,7}.

This similarity of activity suggests the possibility of using the fungi as quick tests for the evaluation of new antiviral compounds following the same procedure used in the evaluation of the antibacterial activity of the antibiotics.

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Control of Glycolipid Synthesis in a Cultured Hamster Cell Line

THE synthesis of complex ceramide glycolipids can be depressed in virus-transformed animal cell lines. The initial observation was made when Hakamori and Murakami¹ showed that polyoma virus-transformed BHK21 cells contain less haematoside than untransformed cells. Mora *et al.*² found in subconfluent cultures of mouse cell lines that concentrations of haematoside were comparable in spontaneously transformed and untransformed lines but that SV40 virus transformation led to a decrease in the concentrations of other gangliosides. We have found that transformation of NIL2 hamster cells leads to a depression in the synthesis of three glycolipids. The synthesis of these same three specific components may, however, be sub-optimal in normal NIL2 cells kept in an actively growing non-contact inhibited state.

NIL2 cells³ were grown by standard methods in Eagle's medium with 10% foetal calf serum. Lipids were labelled by growing cells for 2 days in the presence of 1-¹⁴C-palmitate (1.3 $\mu\text{Ci/ml}$, 55 $\mu\text{Ci}/\mu\text{mol}$). Cell sheets were washed with phosphate-buffered saline and stored at -20° C before analysis. Cells were removed by scraping and plates were washed with methanol. After drying, the cell residue was extracted with chloroform-methanol (2:1) and chromatographed on thin-layer silica gel plates by the method of Gray⁴. An autoradiograph of a typical chromatogram is shown in Fig. 1.

To test the effect of cell density on glycolipid synthesis, cells were plated at high ($5 \times 10^4 \text{ cm}^{-2}$) and low ($5 \times 10^3 \text{ cm}^{-2}$) density on segments in the same 9 cm Petri dish separated initially by a ridge of melted plastic. After incubation overnight to allow attachment, the medium was made confluent and labelled palmitate was added. After 2 days of labelling and growth at 37° C, cells from the two areas of the plate were counted and extracted separately. Comparisons were made with extracts from equal numbers of cells. After chromatography and autoradiography the radioactive areas were removed from the thin-layer plates and counted. The results of such an experiment are shown in Table 1. Although approximately equal labelling occurred in the principal phospholipids and also in haematoside (GM₃) and ceramide dihexoside (CDH) it is clear that in cells growing at the lower cell density there is much less incorporation into ceramide trihexoside, galactosylgalactosylglucosyl ceramide (CTH), the aminoglycolipid, β -N-acetylgalactosaminylgalactosylgalactosylglucosyl ceramide (AGL) and the unidentified ceramide (CX).

Similar incorporation experiments were carried out with NIL2 cells transformed by hamster sarcoma virus⁵ and an adeno 7/SV40 hybrid virus. In both cases it was found that there was normal synthesis of phospholipids and of haematoside and ceramide dihexoside. Little or no CTH, AGL or CX could be found, however, in these transformed lines. It is interesting that the same three glycolipids, and only these

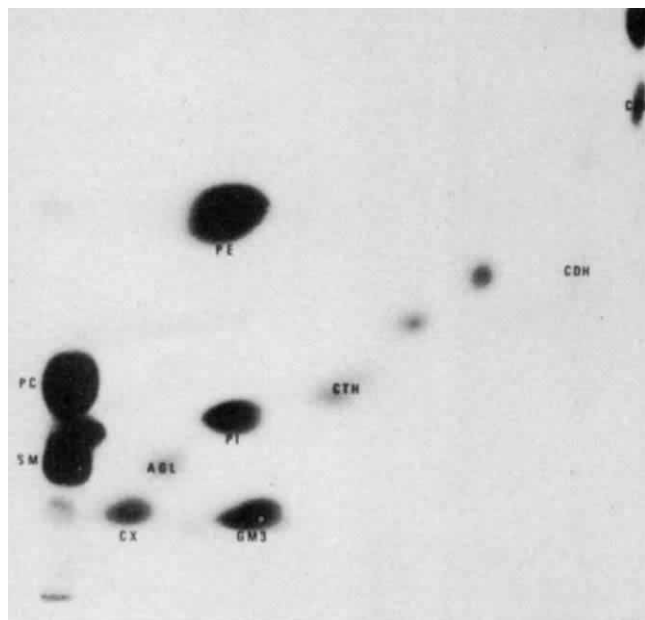


Fig. 1 Autoradiograph of a thin-layer chromatogram of NIL2 cells labelled with $1\text{-}^{14}\text{C}$ -palmitate. The origin is at the lower left. Fatty acids and neutral glycerides run at the upper right corner. SM, Sphingomyelin; PC, phosphatidyl choline; PE, phosphatidyl ethanolamine; PI, phosphatidyl inositol; CX, an unknown ceramide that generates ceramide dihexoside on partial acid hydrolysis; GM₃, haematoside; AGL, ceramide tetrahexoside; CTH, ceramide trihexoside; CDH, ceramide dihexoside; and CMH, ceramide monohexoside.

three, are synthesized more actively by contact inhibited cells than by sparse untransformed NIL2 cells. The result suggests that the lack of these complex glycolipids in transformed NIL2 cells could simply be a reflexion of the lack of normal contact inhibition and lack of growth restraint in transformed cells. A full report will be published elsewhere⁶.

Table 1 Incorporation of $1\text{-}^{14}\text{C}$ -Palmitate into Glycolipids and Phospholipids of NIL2 Cells

Lipid *	Incorporation (c.p.m. $\times 10^{-3}$)	
	Low cell density area	High cell density area
PC+SM	928	1,071
PE	187	165
CX	3.5	13.6
GM ₃	23.6	34.7
AGL	1.0	10.6
CTH	2.6	9.5
CDH	0.7	0.8

Cells were labelled for 2 days with high and low density areas on the same 9 cm Petri dish as described in the text. After extraction, chromatography and autoradiography, the autoradiograph pattern was used as a template for removing spots for scintillation counting.

* See Fig. 1 legend for abbreviations.

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Segregation of Univalents on Mini Spindles

MANY authors have reported that the behaviour of univalent chromosomes at meiosis is irregular. At metaphase they tend to lie off the metaphase plate and closer to the poles than the bivalents; and it has been suggested that this is because the univalents move to the poles earlier. In the triploid species *Leucopogon juniperinus* univalents are close to the poles at metaphase, but serial sections show that they are not in the same plane as the spindle on which the bivalents are positioned (Fig. 1). Closer examination of the metaphase cells shows that the univalents are attached to a separate, much reduced spindle, which is attached to the same pole as the "bivalent" spindle but is formed in a different plane (Fig. 1, cells 2 and 3).

This observation suggests that the difference in behaviour of the chromosomes is associated with their lack of pairing. If in a plant which normally has one accessory chromosome (univalent at meiosis), this chromosome becomes doubled, then the two homologous chromosomes can pair in meiosis and behave on the metaphase plate as a normal bivalent¹. Similar behaviour has been reported for the unpaired X chromosome in the mantid *Humbertiella indica*, in which the univalent X was attached to only one pole of the meiotic spindle. In abnormal cells in which the X had precociously divided, sex bivalents were formed which behaved normally on the spindle². So this unusual behaviour of univalents at meiosis results not

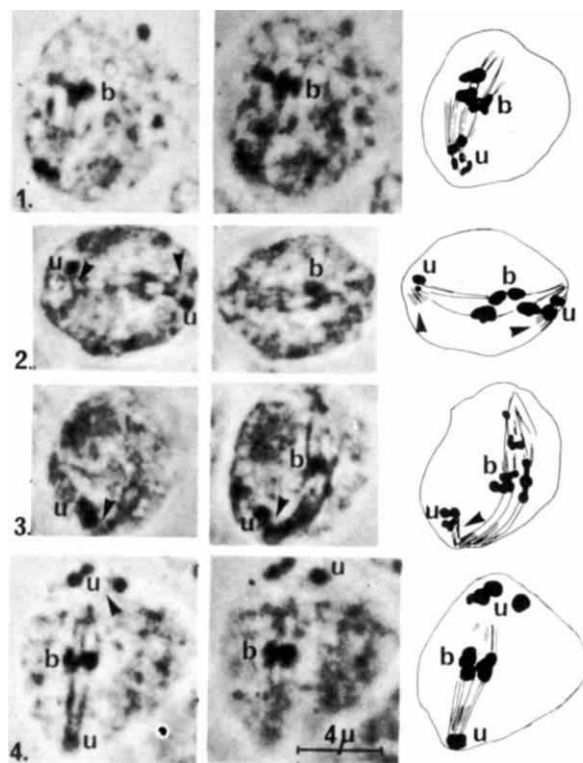


Fig. 1 Chromosomes of *L. juniperinus* during metaphase.

from the properties of individual chromosomes but from their unpaired state.

In most plant species the behaviour of univalents is non-random in the embryo sac mother cell and random in pollen mother cells^{3,4}; in *Leucopogon juniperinus*, however, it is non-random in both⁵. During microsporogenesis, at anaphase 1, all four univalents go to one pole with a frequency of 55.7% compared with a random expectation of 12.5%. Because there is a cytoplasmic gradient in embryo sac mother cells and it has been deduced that there is a gradient in the pollen mother cells of *Leucopogon*, it is very likely that non-random behaviour of univalents is in response to a cytoplasmic gradient.

The univalents in *L. juniperinus* are arranged on their small spindles at the poles when the bivalents move on the metaphase plate, so that their response to the cytoplasmic gradient must occur before metaphase. The response to the cytoplasmic gradient determines not only the unequal segregation of univalent chromosomes but also whether the small spindles will be set up at one or other or both poles.

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DDE reduces Medullary Bone Formation in Birds

DURING the past two decades residues of certain chlorinated hydrocarbons, especially DDT, have caused declines in the populations of various carnivorous birds in the North Temperate Zone by reducing their reproductive success¹⁻³. Contaminated birds lay eggs with abnormally thin, insufficiently calcified shells, so that there is increased egg breakage and embryonic death⁴⁻⁹. Although adult mortality, abnormal behaviour, delayed ovulation and nesting, egg eating, and failure to lay eggs also sometimes result from such contamination^{1-3,8-11}, the thin eggshell phenomenon is the chief cause of the declines in population^{3,6,8}.

Chlorinated hydrocarbons induce hepatic microsomal enzymes that hydroxylate steroids^{12,13}, including oestrogens, which are produced in increased amounts by the avian ovary before egg laying. In birds of both sexes, oestrogens mediate deposition of calcium in the medullaries, or hollow parts of the skeleton¹⁴, where it serves as a labile calcium source for eggshell formation. Chlorinated hydrocarbons should therefore reduce medullary bone formation as well as eggshell calcification. We have investigated this possibility by injecting an oestrogen into male pigeons and determining whether the ingestion of chlorinated hydrocarbons by some of these birds reduces medullary bone formation. *p,p'*-DDE[1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene] was used because it is the most widespread chlorinated hydrocarbon pollutant, and it has a substantial effect on eggshell thickness.

Seven groups, each of four 5 yr old male silver king pigeons, were injected twice weekly with doses of β -oestradiol ranging from 0.05 to 0.70 mg per day during the spring of 1969. At each dose, two birds received feed containing 100 p.p.m. of DDE dissolved in corn oil, and two control birds received feed with an equal amount of corn oil. At the end of 4 weeks, all birds were decapitated, and both femurs were removed,

calcined at 675° for 8 h, and weighed. The average combined weight of both femurs of ten other 5 yr old male pigeons of comparable weights given neither oestradiol nor DDE was 0.793 g. This value was subtracted from all femur weights of experimental birds to give the medullary bone weights (Table 1).

Table 1 Femur Medullary Bone Weights

β -Oestradiol (mg/day)	Control birds (g)		DDE birds (g)	
0.05	0.284	0.393	0.213	0.139
0.10	0.201	-0.060	0.219	0.037
0.20	0.201	0.164	0.165	0.123
0.30	0.227	0.409	0.120	0.110
0.40	0.324	0.293	0.037	0.109
0.50	0.405	0.315	0.125	0.275
0.70	0.444	0.355	0.264	0.126
Overall mean weights	0.283 g		0.147 g	
Expressed in %	100%		52.1%	

Medullary bone formation as a function of the dose of oestradiol was inconclusive, but when the data were pooled for the two groups, medullary bone formation by the birds fed DDE was only 52.1% as much by weight as that in control birds. The difference between the two groups was significant at the 0.01 level according to the Mann-Whitney U test¹⁵. This finding is consistent with the reduced level of circulating oestradiol found by Peakall and believed to result from induced hepatic hydroxylation⁹. Enzyme induction would also explain the altered behaviour, failure to lay, and late ovulation and nesting occurring among the carnivorous birds^{3,9}. Peakall and Bitman have presented convincing evidence, however, that the thin-shelled eggs are caused primarily by inhibition of carbonic anhydrase, an enzyme required for shell formation in the shell-forming region of the oviduct^{3,7,9}. The diminished reproductive success of these birds is therefore explainable by the simultaneous occurrence of enzyme induction in the liver and enzyme inhibition in the oviduct, both resulting from these chlorinated hydrocarbon pollutants.

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Method for Measuring the Leaf Surface Area of Complex Shoots

A KNOWLEDGE of leaf surface area is essential for many plant physiological and ecological studies¹⁻⁵. Conventional measurements based on leaf dimensions are invariably laborious and often only approximate. Other methods aimed at increasing the speed and accuracy of the measurements, such as photoelectric techniques^{6,7}, are only really applicable to broad leaved species. For microphyllous and needle leaved species the only reliable method so far has been to calculate the surface areas of selected leaf samples from measurements of length and circumference, then to extrapolate the values to whole shoots on the basis of leaf numbers or fresh weights^{5,8}. Doronichev⁹ has attempted to simplify the measurements for conifer shoots by determining the adsorption of methylene blue from aqueous solutions on the assumption that a monomolecular layer is formed on the surface and that each mg methylene blue adsorbed corresponds to a surface area of 1.05 m². For most plant shoots, however, the change in methylene blue concentration is far too small to be accurately measured using standard photo-densitometers.

We have developed a method on somewhat similar principles that is much more applicable for general use. A shoot is removed and thinly coated with the pressure sensitive adhesive, 'Adsol 400' (Adhesive Solutions Ltd, Rickmansworth), by dipping it two or three times into a solution diluted 1 : 7 by weight with benzene. After about 5 min, to allow the benzene to evaporate, the shoot is weighed and then covered with small Ballotini glass balls (Jencons (Scientific) Ltd, Hemel Hempstead) by pouring the balls over the shoot whilst it is slowly rotated. The shoot is then vigorously tapped or shaken to remove loose balls and reweighed. The balls form a uniform layer over the whole of the exposed surface (Fig. 1), so the gain in weight is directly proportional to the area covered. Leaf and stem surface areas can be separated by removing the needles and repeating the exercise on the stem only, after washing off the balls and adhesive with benzene.

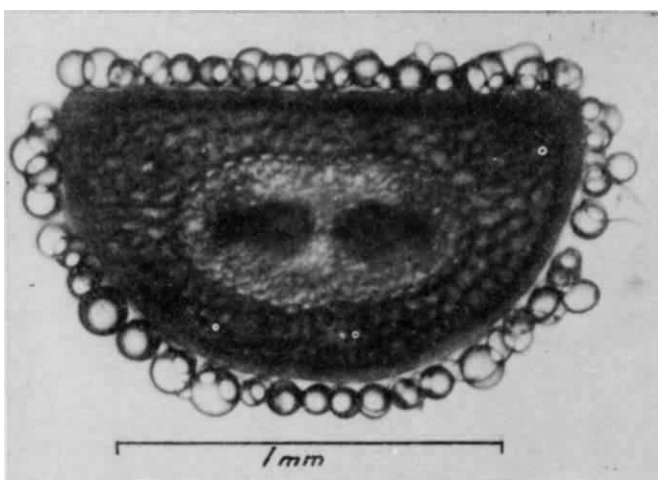


Fig. 1 T. S. Corsican pine needle coated with Ballotini glass balls.

Tests on a range of artificial flat and cylindrical surfaces showed that balls of approximately 0.11 mm diameter gave the best compromise between a large weight increase per unit surface area and a more consistent packing distribution. For this size of glass ball, the gain in weight was $13.6 \pm 0.1 \text{ mg cm}^{-2}$.

For several Norway spruce shoots (single needles), leaf surface areas determined by the glass ball method and ranging from 17 to 30 cm² agreed to within 3% (s.e. $\pm 1.4\%$) with those calculated from the dimensions of a 15% random sample of

needles. For each shoot, the glass ball method took 10–15 min, the conventional method several hours. In the case of mature or near mature Scots pine shoots, the situation is rather more complicated because most of the paired needles are separated at various distances from the base so that the exposed needle surface area as measured by the glass balls is less than the total surface area. When allowance was made for this in the direct measurements, the two methods again agreed to within 3% (s.e. $\pm 0.1\%$) for areas of 26 to 34 cm². In many physiological studies, for example, those concerned with gaseous exchange or evaporation, a knowledge of the exposed area of leaf surface is probably more relevant than that of the total surface area. The method can be readily adapted, however, to give total leaf surface areas, for example, by removing one of the needles from each pair so that half the total leaf surface area can be determined.

This new method is simple, rapid and, as far as we can judge, accurate; because it is non-destructive, measurements can be replicated on the same shoot. It can also be used for other complex structures, provided that these are sufficiently rigid to prevent adhesion between surfaces when the adhesive is applied. Different Ballotini ball grades can be chosen according to the detail of the surfaces studied and the precision required. It is important in practice to use dilute solutions to avoid loss of surface detail through the accumulation of the adhesive; with the ridged stems of Scots pine, for example, covering with adhesive decreased the circumference by about 4%. Because of the need to ensure a complete and uniform coating of all surfaces with the balls, a fluidized air bed method may prove more effective than the simple pouring system used here; but our experience has been that the latter method is satisfactory for most purposes.

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Bats and Fog

ON windless evenings fog commonly forms in dense, sharply defined patches, especially in sheltered bays of ponds. As the evening progresses and the temperature falls, these patches may grow and coalesce, advancing over the pond but maintaining a sharp front at which visibility changes profoundly within a few metres. In such conditions insectivorous bats hunting over the water have been observed to turn back at the fog front as if at a solid wall, even though their hunting area may become severely restricted. This behaviour suggests that fog may have a direct effect on echo location.

Meteorological studies^{1,2} have shown that stable fog consists of water drops with diameters ranging from about 1 μm to about 100 μm . The range of size varies in different fogs but is always rather wide because of coalescence. Drops smaller than 1 μm form a "blue haze" due to selective Tyndall scattering of shorter light wavelengths; drops from 100 to 400 μm fall steadily as "drizzle" while drops from 400 to 1,000 μm form "rain", although much larger drops may be formed in thundery showers.

In 1896 Rayleigh³, discussing the influence of fog on the transmission of audible sounds, wrote, "In spite of isolated assertions to the contrary, it was generally believed . . . that the influence of fog was prejudicial. Tyndall's observations prove satisfactorily that this opinion is erroneous, and that the passage of sound is favoured by the homogeneous condition of the atmosphere which is the usual concomitant of foggy weather". Furthermore, ". . . the disturbance of plane sonorous waves by a small obstacle . . . depends upon the ratio of the diameter of the obstacle to the wavelength of the sound". The wavelengths of the ultrasonic spectrum of bats range from a little more than 2 mm to about 20 mm, as shown by the double ordinate scale of Fig. 1 (upper). Even the largest fog drops thus have a diameter which is only 1/20 of the shortest wavelengths used by bats and 1/70 of the wavelength at 50 kHz. The presence of fog should therefore produce little disturbance by scattering of bat sounds.

Rayleigh also showed, however, that liquid drops resonate mechanically at frequencies dependent on their dimensions. His formula simplifies for spherical water drops in air to approximately

$$f = \left(\frac{500}{d} \right)^{1.5}$$

where f is the resonant frequency in kHz and d is drop diameter in μm . This relation is shown in Fig. 1 together with ranges of drop size for three natural fogs, plotted from data given by Houghton and Radford¹. It is convenient to consider the frequency band used by bats as 15–150 kHz in general, corresponding to droplet sizes from 82 μm to 18 μm . The range of frequencies for British species is covered by droplet sizes from 70 μm (about 20 kHz) to 22 μm (110 kHz).

Fog containing droplets in this range will theoretically have a strong influence on the propagation of echo location signals from a bat. Each droplet will absorb sound energy at its resonant frequency and will subsequently reradiate it over a relatively long time. Thus there will be no immediate and sharp echo return but a slowly decaying "ringing", as from a struck bell. Although each droplet will be sharply tuned because of its almost perfect spherical shape, the effect of any given fog will be spread over a frequency range that depends on the spectrum of droplet sizes present. The fog will thus be opaque to ultrasound as to light, but with one major difference. The droplets are large compared with light wavelengths so that all colours are scattered and fog appears white in, say, car headlamps; but to an ultrasonic echo location system it must be a "black void" with perhaps a faint persistent afterglow. Not only would insect detection become difficult or impossible but there would be a danger of colliding with obstacles or with the ground or water below.

To demonstrate these effects, some simple physical experiments have been performed in the laboratory. Artificial, dense, white fog may easily be produced by dropping small lumps of solid carbon dioxide (cardice) into warm water. The fog is cold and rapidly fills its container until it pours over the edges and rolls across the bench. An ultrasonic loudspeaker was placed in such a vessel facing a calibrated microphone 13 cm away, and short pulses of pure tones were transmitted between the two. The intensity of the signal received in clear air was then compared with that received through thick fog at a number of different frequencies. The amount of attenuation produced by the fog was high and

increased with frequency from about 40 dB/m at 20 kHz to 130 dB/m at 80 kHz and to about 190 dB/m (difficult to measure accurately even over 13 cm) at 100 kHz. This means that two of the loudest bats would be inaudible to each other at distances over which detection of faint insect echoes is possible in clear air. Admittedly this was a very dense fog with a "visibility" of only a few centimetres and natural fogs would be unlikely to give such startling values. On the other hand, the spectrum of drop sizes of the artificial fog probably has a peak at a smaller drop diameter than the natural fogs of Fig. 1, for maximum attenuation apparently occurred above 100 kHz.

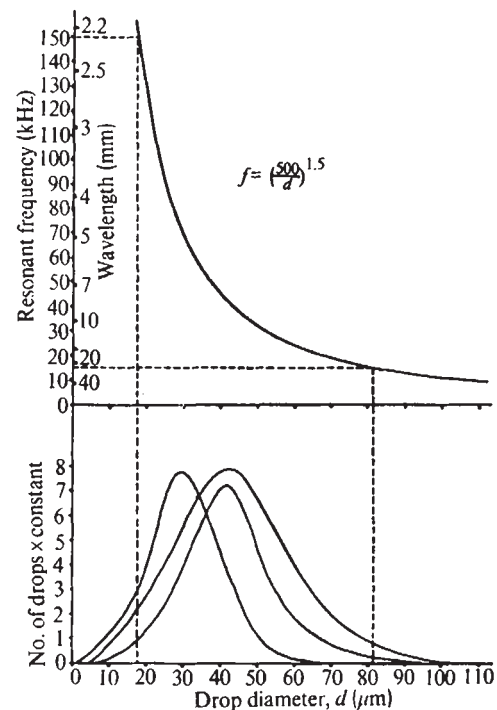


Fig. 1 Above, the resonant frequencies of spherical water drops in air, calculated by a formula derived from Rayleigh³. Below, spectrum of drop sizes for three fogs, replotted from volume distribution curves given by Houghton and Radford¹. The vertical dotted lines delimit the drop sizes resonant between 15 kHz and 150 kHz.

In another arrangement the loudspeaker and microphone were aimed downwards, well above the container, so that transmitted pulses were received after reflexion from the water surface. The pulse generator triggered the time-base of an oscilloscope which then displayed the strong specular echo after the correct propagation delay. When a little cardice was added, the container filled with fog to the brim and the echoes were attenuated accordingly. But no earlier echo could be detected from the smooth surface of the fog. The beamed sound was simply absorbed. Subsequent reradiation of this sound by the droplets could not be detected, suggesting that the droplets are very sharply tuned. The ears of bats are much more sensitive than microphones and might be able to detect this ringing which would form a further source of confusion.

The ecological implications of all this are clear. Insectivorous bats are in any case unlikely to profit by flying in generally foggy conditions because of the paucity of food. Discrete fog patches may develop when hunting is good but it would be dangerous as well as unprofitable for a bat to enter such a bank even if its prey flies into one.

The influence of rain is also worth considering. Bats may be seen hunting in drizzle, though often in a tentative, half-

hearted manner. Steady drizzle deters insect flight but there would seem to be no serious hazard to echo location. Sound scattering will still be slight and even the finest drizzle droplets will resonate below 10 kHz. In the sudden, heavy rain of thunderstorms there may be large numbers of insects in the air and bats are often seen to continue active and apparently successful hunting, with rapid turns accompanied by ultrasonic "interception buzzes". Drops of 1,000 μm diameter resonate at 350 Hz but scattering may be appreciable, especially at the highest, "blue" frequencies. The problem is then one of distinguishing insect echoes from the "clutter" of echoes returned by raindrops. The critical difference may be that the drops all fall downwards and maintain a constant reflectivity, whereas flying insects do neither. The work of Webster⁴ suggests that the processing of echo signals by bats is sufficiently sophisticated to deal with this situation and this is certainly supported by field observation.

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pH of Very Acid Soils

THE purpose of this note is to call attention to the fact that usual methods of measuring soil pH¹ seriously underestimate the pH of very acid soils, such as those of coal mine spoils², cat clays³ and solfataras⁴, in which acidity is due to the presence

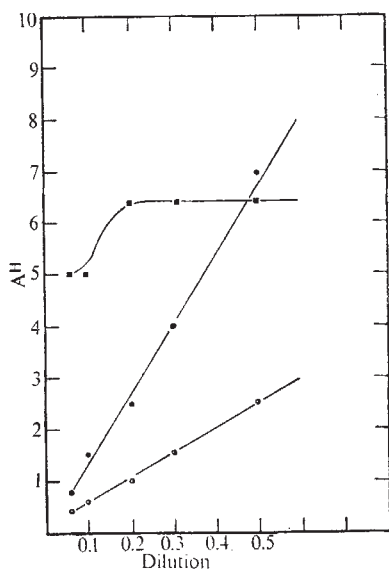


Fig. 1 The dilution curves of three soils. ■, Clay soil, pH=5.3; ●, solfataras soil, pH=1.90; ○, mine waste soil, pH=1.30.

of free sulphuric acid. Standard methods for measuring soil pH involve making a slurry of soil with (usually) distilled water at a 1 : 2, 1 : 5, or 1 : 10 dilution, and reading the pH of this slurry. Implicit in this procedure is the assumption that the soil is buffered and hence that pH does not change with dilution. This assumption is erroneous in the case of the sulphuric acid soils.

In our work on the microbiology of very acid soils⁵ we wanted to know the pH values to which the microorganisms were actually subjected; that is, the pH of the soil water. To measure this, a slurry of equal parts of soil and water was made and from this slurry a series of dilutions in water were made. The pH of each dilution was measured using a Corning combination glass electrode, and a graph was prepared relating hydrogen ion concentration to dilution (Fig. 1). In the case of the sulphuric acid soils, a straight line was generally obtained and this line was then extrapolated back to zero dilution and the hydrogen ion concentration of the soil obtained. If the pH of the soil water was desired, the moisture content of the soil was determined and the dilutions then corrected to represent dilutions of the soil. (For example, if the moisture content of the soil were 10% then the initial dilution would be 1 : 20 rather than 1 : 2.) As also shown in Fig. 1, an acidic agricultural soil, being buffered, does not change pH significantly with dilution, and hence its pH can readily be estimated by the standard procedure.

Table 1 pH of Coal Mine Refuse from Pike County, Indiana

Diluent	Method		Estimated pH at zero dilution	
	1 : 2 dilution	1 : 10 dilution	Soil	Soil water
Distilled water	3.8	4.5	3.5	3.4
1 M KCl	2.3	2.9	—	—
0.01 M CaCl ₂	2.7	3.2	—	—

Our new procedure was compared with standard procedures for several coal mine spoil and solfataras soils. The results with one representative soil are shown in Table 1. It can be seen that the pH value as measured is lower than estimated by standard dilution in distilled water. The pH obtained by standard dilution in KCl or CaCl₂ is lower than that obtained by our method, but reflects exchange of hydrogen ions by diluent cations¹ and hence does not necessarily represent the pH of the soil water. When considering the introduction of plants on coal mine spoils, cat clays, or other very acidic soils, a knowledge of the exact pH value, as determined by our new method, should be of significant value.

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BOOK REVIEWS

Second Time Around

Nature and Man: Essays Scientific and Philosophical. By William B. Carpenter. Pp. vi+483. (Gregg International: Farnborough, Hants, 1970. First published 1888.) \$20.20; £8.40.

Social Statics: or the Conditions Essential to Human Happiness Specified, and the First of Them Developed. By Herbert Spencer. Pp. viii+476. (Gregg International: Farnborough, Hants, 1970. First published 1851.) \$18.75; £7.80.

The Wonderful Century: Its Successes and Its Failures. By Alfred Russel Wallace. Pp. xii+400+12 diagrams. (Gregg International: Farnborough, Hants, 1970. First published 1898.) \$12.95; £5.40.

The Biographical History of Philosophy from Its Origin in Greece Down to the Present Day. By George Henry Lewes. Pp. xxxvi+675. (Gregg International: Farnborough, Hants, 1970. First published 1857.) \$24.50; £10.20.

The Constitution of Man Considered in Relation to External Objects. By George Combe. Eighth edition, revised, corrected and enlarged. Pp. xx+507. (Gregg International: Farnborough, Hants, 1970. First published 1847.)

LIKE many British historians, I greeted the first announcement of Gregg International's reprint series of nineteenth century classics with some enthusiasm. One of the most attractive features of this new venture is the emphasis on works illustrating the period's concern with the social and philosophical implications of pre- and post-Darwinian biology.

The need for re-publication of such titles as the five under review is undisputable. Most of them have been out of print for well over half a century, during which time there has been a remarkable upsurge of interest in Victorian intellectual history. Yet, for students and scholars in residence at universities constructed since the First World War, such books are virtually unobtainable. Research is accordingly hamstrung and, more important, it becomes impossible to assign to students primary sources, which, in the view of teachers like myself, are often preferable to existing secondary accounts.

Thus courses in the social thought of nineteenth century Britain would greatly benefit from having these volumes by Carpenter, Combe, Lewes, Spencer and Wallace included on their reading lists. On the question of positivism's 'curious

effect' upon Victorian thinkers, one could do far worse than consult the 'Eleventh Epoch' of Lewes's *History*, "Philosophy finally relinquishing its Place in favour of Positive Science." The decline of phrenology could be traced through the works of Combe, Carpenter and Wallace. Even more fascinating would be a comparison between the diametrically opposed sociopolitical views of those two Darwinians before the name, Spencer and Wallace. The Gregg series, in short, would soon to hold great promise.

But there is a snag. Excluding the cost of *The Constitution of Man*, the price of the four remaining books comes to £31.80 (\$76.40). I honestly don't understand how production costs could justify such an abnormally high figure. The volumes are unedited, facsimile offprints of works whose copyrights have long since expired. Even the bindings, serviceable though they may be, are nothing out of the ordinary. The real question, however, is: who can afford the expenditure of so much money for apparently so little in return? Presumably the libraries of newer American universities can manage such an outlay, but corresponding institutions in Britain will have to think twice (and economize elsewhere) before making their purchases. Individual scholars, on the other hand, probably fall into two categories. Those affluent enough to buy reprints at such prices can undoubtedly afford, if not the first, then at least a later edition of the original. As for the remainder of academics, myself included, acquisition of any one of the Gregg publications is financially out of the question. Needless to say, this is a great pity.

PAUL GARY WERSKEY

Prospect of Perfection

The Perfectibility of Man. By John Passmore. Pp. 396. (Duckworth: London, October 1970.) £4.20.

To some of us in these days, the idea of perfectibility in man seems perhaps a sad illusion or a sick joke. But it has been far from a joke for many earnest thinkers in the past, and it may still prove to be a quite compelling illusion for multitudes in the future. For humanity has always sought consolation in its sufferings from one illusion or another of which persuasive voices have been able to convince it; persuasive if not at all disinterested voices.

The consequences of a belief in per-

fectibility are therefore enough to justify Professor Passmore's inquiry into its symptoms and expression. But what is the perfectibility that is believed in? This is what he wisely refrains from telling us. It is something benevolently attainable by effort, by education, by conversion, by election, by heredity, by evolution. It is something fortunately attainable by individuals, by societies, by classes or by races. Or not attainable. It is something which the priest or the prophet or the political philosopher often judges by its effects in improving or controlling the behaviour of those who hear and obey, such effects being subject to the prevailing temper, bold and optimistic, or pessimistic and timid, of the time and place and people. For as Teilhard de Chardin wrote, and Karl Marx and many of his disciples might have written, "Men must believe that mankind is perfectible, since otherwise human effort will collapse".

Scientists no doubt often feel like that, and by taking drugs, as Professor Passmore suggests, could always feel so. But when they write they are usually more careful. They observe certain rules, but these rules have allowed them to reach conclusions which would be unbelievable had not our author most authentically collected and quoted them. When Francis Galton explains that men could be selected as superior to white men as white men are to negroes, we are surprised. When H. J. Muller more recently foresees "modes of thought and living that would today seem inconceivably godlike", we are more surprised. But what surprises us most, and most instructively, is the sentence in which Darwin almost concludes the *Origin of Species*. This is a sentence which introduces his view of perfectibility and it escaped unscathed the successive recensions of his book: "As natural selection works solely by and for the good of each being, all corporeal and mental endowments will tend to progress towards perfection".

Five years later, Alfred Russel Wallace was able to fill in the details of Darwin's picture. In his view, man would become a "single homogeneous race" corresponding in character with "the noblest specimens of existing humanity". In other words, we shall not all move forward together as Galton imagined but those behind will catch up. Trotsky, much later, was to express the same hope or faith. It was the correct view for the Marxist as well as the Darwinian.

Professor Passmore does not take the scientific argument beyond this Darwinian point. He merely concludes that although mankind may never be perfect, men (and perhaps women) might well try to do better. But it is worth our while noting how far the views of Darwin and Galton, as well as of Marx and Trotsky, might be connected with the scientific evidence available to us.

In the first place today we are faced with the collapse of Lamarckian assumptions. Their infinite scope for wish fulfilment and dictatorial exploitation, priestly and secular, is lost. This leaves the mystical and also the political perfectibilist without his old scientific ground to stand on. In the second place, our ideas about natural selection make Darwin's argument look very shaky. Today we do not see natural selection working just "for the good of each being". On the contrary, we see it often subordinating the individual to the needs of the community and the requirements of the breeding system. We also see it operating within a framework which chemically and mechanically is most refractory. For example, we have to put up with twenty-three chromosomes: is this a magic number? Is homozygosity the perfect state of man, or even of woman?

Perhaps the most striking change in our beliefs concerns uniformity. The notion of a community or a species which is entirely without differences, individual or racial, social or sexual, implies utter stability and utter stagnation. It has always been abominable. It has now also become inconceivable. How should we get on without our genetic load?

Where then will the perfectibilist take his last stand? The environment would seem to be his safest refuge. Man has learnt to control his physical environment. He has indeed frequently been heard to boast of his unique powers in this respect. But as he has not learnt to control his genetic environment, which depends on his own breeding in quality or quantity, his physical accomplishment has become a destructive asset. We cannot therefore hope for a speedy millenium. But neither, fortunately, need we fear it.

Professor Passmore does not say these things. But he is sceptical enough to approve of them. The only fault in his book is that it lacks arrangement and therefore continuity. His work was not planned. It swept its author along. It turned out to be an encyclopaedia which takes him and us through the burrows and warrens of error and fraud, following each new rabbit that he uncovers and pursuing it to the last indefatigable but fatiguing footnote. It may be a long time before anybody pursues these things further or in such small print.

C. D. DARLINGTON

Botanical Walkabout

Allan Cunningham: Botanist and Explorer. By W. G. McMinn. Pp. 147 + 4 plates. (Melbourne University: Carlton, Victoria; International Scholarly Book Services: London. December 1970.) \$4.20; £2.00.

THE huge unexplored continent of Australia of the nineteenth century offering a challenging, unique flora and fauna sets the background for W. G. McMinn's study of Allan Cunningham, undoubtedly one of Australia's greatest botanical collectors. The author in his preface disclaims any attempt to assess or analyse Cunningham's scientific ability, but on the other hand makes no apology for offering a study of the man. Although Allan Cunningham is portrayed with great sympathy and feeling the effect is a rather formal historical work containing considerable information on early exploration in Australia.

The author shows excellent insight into the mind and character of the systematic naturalist, and readers from disciplines other than botany may be interested and enjoy this study. As a readable botanical narrative, however, it is a disappointment, for little use is made of Cunningham's detailed and fascinating botanical journals. In comparison with Ida Lee's *Early Explorers in Australia*, I feel there is a lack of balance between explorer and botanist.

The introductory chapters read well, describing Allan Cunningham as an insecure young man lacking in self assurance, attributable to his rather humble background. Following his contact with and commission by Sir Joseph Banks to make botanical collections for Kew, his confidence gradually grew into scholarly diffidence and quiet unexpansiveness. Later chapters outline his exploration, detailing, perhaps too fully, his travels and recounting his thoughts, activities and achievements as a botanical collector but superficially. The gradual growth of confidence with experience and success turned, with failing health, to disillusionment and discontent. Some of the journeys could have been presented more clearly by the inclusion of more and better maps.

In the final chapter the author, in summarizing Cunningham's character, comments on his diligence and industry by referring to the tireless walks in search of orchids, and his careful follow up of the results achieved at Kew with his seeds and seedlings; and on his sensitivity by reference to his writing on *Acacia podolyriaefolia*. These generalizations, although undoubtedly derived from Cunningham's journals, are insufficiently exemplified in the principal part of the work. It is a pity that McMinn did not expand the botanical aspect of this study a little more fully,

because as a result one is left with a feeling that the work lacks depth. The extensive references and bibliography clearly indicate exhaustive research and will be undoubtedly of value to the student.

I. K. FERGUSON

Freshwater Sediments

Non-Marine Organic Geochemistry. By Frederick M. Swain. (Cambridge Earth Science Series.) Pp. xii + 445. (Cambridge University: London, October 1970.) £10.00; \$32.50.

THIS volume gathers together many data on the nature and variation of organic matter in freshwater sediments that will be of use to organic geochemists working in widely differing fields. The book is, however, a good illustration of the difficulties—even for an experienced and well-regarded scientist—of writing a balanced, comprehensive review of a scientific field, which, if not undergoing explosive expansion, is certainly developing with vigour. Dr Swain's new book does not change the view that up to now the edited book, with chapters by a number of authors, has been the more successful presentation in the detailed discussion and evaluation of the different facets of organic geochemistry.

The first chapter of *Non-Marine Organic Geochemistry* is a necessary survey of organic materials in the geological environment, which is unfortunately marred, as are other chapters, by numerous errors in structural formulae. The more authoritative parts of the book, the chapters on bitumens, protein amino-acids, carbohydrates and organic pigments of non-marine sediments, comprising almost half of the text, rely heavily on the researches of Swain and his co-workers. These chapters carry most critical comment, although more contrasts could usefully have been made with, for example, the character and behaviour of organic materials in other environments. Chapters on field and laboratory analysis of organic materials and on the characteristics of non-marine sediments are also considerably influenced by the author's work. Away from Swain's chief interests, the book becomes much more a matter of report. The chapter on non-marine coals is weak, and so unbalanced in form and content that the contribution is misleading. Furthermore, many of the coals considered, particularly those of the paralic coal-fields, must certainly have been at least partly influenced by marine or near-marine conditions. The book also contains appendices giving solvent systems and R_f values for paper and thin-layer chromatography, thirty pages of references and adequate subject and author indices.

The editors must exert more control on their printers to ensure a higher quality of production in the rest of the series. Absorption spectra should not overlap figure margins. The smudging and persistent variation on many pages of the ink density of chemical formulae and resonance structures of benzene should not have been allowed, and the quite inexplicable changes in type width give what must surely be an unintended significance to certain chemical reactions. These deficiencies are, however, chiefly in the first fifty pages of the text, and the general impression of type and figure lay-out of the volume is pleasing.

DUNCAN MURCHISON

Drug Data

Sympathomimetic Drugs. By Domingo M. Aviado. (A Monograph in the Bannerstone Division of American Lectures in Anesthesiology.) Pp. xix + 613. (Thomas: Springfield, Illinois, July 1970.) \$40.

THIS book has been compiled for medical students, postgraduate students and doctors. It aims to assist doctors whether working in hospital or outside. Owing to the pruning of the time available for teaching pharmacology to medical students in Philadelphia, USA, the text deals less with general pharmacological principles arising from extensive courses in practical pharmacology, and more with clinical uses. Because of this pressure of circumstance, the author plunges the reader into the deep end, dealing in detail in chapters 1 to 5, 7, 8 and 10 with eight of the sympathomimetic drugs most commonly used in the US, namely epinephrine (adrenaline), norepinephrine (noradrenaline), ephedrine, metaraminol, mephentermine (mephenteramine), phenylephrine, methoxamine and isoproterenol (isoprenaline). To UK eyes, this list may seem somewhat strange, but it serves to emphasize that there are national differences when considering the emphasis placed on various drugs by the user communities. Chapters 6, 9 and 11 consider much wider spectra of drugs which might be used for raising blood pressure, cardiac stimulation, nasal decongestion and appetite suppression, vasoconstriction, vasodilation and relaxation of the bronchiolar muscle, against the detailed background information provided for each of the eight archetype sympathomimetic compounds. Each chapter is followed by a short summary of its main points and a substantial reference list.

This type of approach in a textbook would seem to be more useful to the British medical graduate than to the undergraduate, although the latter is invited to start by reading chapter 12

entitled "Pharmacology of Sympathomimetic Drugs" before turning to consider the foregoing chapters. Chapter 12 will enable him "to learn . . . the uses of sympathomimetic drugs in therapeutics". This phrase sums up the approach which is essentially directed towards the practical.

Chapter 12 deals in detail with the pharmacological anatomy and physiology of the sympathetic system before turning to consider α and β receptors and α and β blocking agents. The brief and rather superficial treatment of α and β receptors is disappointing in a book running to over 600 pages, which might be expected to give a wide perspective of its subject. The β blocking agent propranolol receives only passing reference on one page in its own right, and is mentioned on three other pages when referring to interactions with other drugs. Practalol receives no mention. The author, however, devotes much effort to grouping sympathomimetic drugs in Chapter 12 under four headings relating to a direct or indirect action on α and β receptors stimulating the heart and influencing the blood vessels, or acting directly on α receptors (chiefly to constrict blood vessels) or on β receptors (to dilate blood vessels and to relax smooth muscle). He goes on to provide examples of eight clinical situations in which sympathomimetic drugs may be required, ranging from an anaphylaxis, through cardiac stimulation, bronchodilatation and mydriasis to combating shock. The practical approach shows up to great advantage here because the dose and route of administration of each of (often many) alternative drugs are given together with reference to other pages in the book on which the drug is treated in more detail. This type of readily available and systematized practical information is often missing from standard UK textbooks.

Professor Aviado has produced a substantial volume with many references which makes for an unusual presentation of sympathomimetic drugs. He has disciplined himself to take a strict approach severely directed to clinical applications. If the reader is prepared to use the book as a source of such information, he will find much to interest him. No fewer than 386 compounds are tabulated in the final chapter (13). These include the eight considered in detail and 53 in lesser detail in the preceding chapters. In spite of this long list, practalol has escaped inclusion. If the reader is, however, seeking a deep understanding of the mode of action of sympathomimetic drugs, then he will not find the volume helpful for this purpose but he will find the encyclopaedic list of compounds helpful in tracing the structure of less well known compounds.

The author, in his approach, poses

the question "what sort of a book is required" by the medical student and graduate and others working in ancillary fields—a volume answering a host of practical questions or one blending an information source with an understanding of the underlying principles? He is courageous to undertake this task, which will stimulate us to consider our values and requirements in textbooks in this field with particular reference to the growing needs in the UK for extensive educational programmes for postgraduate medical practitioners, young and old alike.

J. P. QUILLIAM

Probing the Brain

Physiological Psychology. By Peter M. Milner. Pp. x + 531. (Holt, Rinehart and Winston: New York and London, 1970.)

THE view that the royal road of advance in physiological psychology involves finding out what happens to an animal's behaviour when one prods around inside its head is widespread. Peter Milner, whose book is the most recent addition to texts on the subject, is evidently of this persuasion and states that "the logic of probing the nervous system for cues (*sic*) to behaviour is almost universally accepted".

The author explains that he is interested in understanding behaviour in the same way that it is possible to understand a motor car or a radio. The difficulty about the probing approach—of which he approves—is that valuable insights about the workings of a radio are not gained by observing its behaviour while thrusting a hot soldering iron into its innards. Even poking about with the terminals of a voltmeter is not going to be much good if we do not already understand how the radio works and what to look for. Comprehending the principles upon which brain mechanisms operate seems to require techniques (such as simulation) which are of a quite different kind.

What one gets from probing is the strong impression that the brain has something to do with behaviour, together with a set of notions about particular parts of the brain being concerned in particular aspects of behaviour. Though much of physiological psychology is still at this stage, the time has come to get away from this kind of approach. Milner makes a modest attempt to do so in that, within the contexts of sensory and motivational systems, he gives a small amount of space to the discussion of possible mechanisms and models. Unfortunately, he does not take this nearly far enough, either in extent or rigour.

This book is one of half a dozen or so such texts available, and is not a bad example of its kind. The author tra-

verses the (by now) familiar field, but does take the trouble to describe most of the experiments that he mentions in sufficient detail for the reader to be able to grasp what was done, and he does adopt a more critical approach than some of his competitors.

KEITH OATLEY

Brain Histochemistry

Macaca mulatta: Enzyme Histochemistry of the Nervous System. By Sohan L. Manocha and Totada R. Shantha. Pp. xii + 348. (Academic: New York and London, August 1970.) £10.05.

THIS work is based on the histochemistry of material from twelve monkeys. The oxidative (monoamine oxidase, succinic and lactic dehydrogenase) and hydrolytic (acid and alkaline phosphatase, ATPase, simple esterase, true and pseudo-cholinesterase) enzymes are investigated using fresh frozen sections. The regions examined include the cerebral cortical areas, the hippocampus, basal ganglia, diencephalon, brain stem, cerebellum, spinal cord, dorsal root ganglia, olfactory bulb, retina, optic nerve and other eye parts, choroid plexus, ependyma and peripheral nerve perineurium. With some two hundred and fifty three micrographs (no electron micrographs) the text is well illustrated although a number of the plates look rather fuzzy—perhaps indicating a need for thinner sections. The material is well laid out, and the introduction to the methods employed should be clearly comprehensible to the novice. The book could well serve as an introduction to brain histochemistry, for the findings are related to numerous references to the literature on corresponding regions in other species (the references stop short, though, at 1968).

Investigators who have kept up to date with the literature in brain fine structure and the localization of transmitter substances will, however, find the discussions disappointing, for in many places the authors seem to have little grasp of these very relevant topics. In the cerebral cortex, for example, they are unaware that most synapses are located on dendritic spines, and that there is growing evidence that (in pyramidal cells) these have an excitatory transmitter. On the other hand, somatic contacts may have mostly inhibitory chemically mediated synapses. The literature on transmitters in the subfornical organ has not really been explored. The presence of choline esterase in dorsal root ganglion cells known to be noncholinergic could have been discussed at much greater length. The cerebellar glomeruli not only contain mossy fibre contacts but a second set—the Golgi cell granule dendrite contacts. The former are excitatory and the latter are inhibitory. Thus we have a dual system which can be precisely pinpointed with the microscope—is it any wonder

that the histochemistry of the cerebellar cortex is in such a state of chaos when topics like this are ignored?

E. G. GRAY

Identifying Yeasts

The Yeasts: a Taxonomic Study. Edited by J. Lodder. Second edition, revised and enlarged. Pp. xvi + 1,385. (North-Holland: Amsterdam and London, 1970.) £27.40.

"THE main intention of this work," says Lodder, "is to produce a book for identifying yeasts." Indeed, anybody now wanting to identify yeasts must have it constantly on his laboratory bench. The fourteen authors, who include most of the leading yeast taxonomists, have apportioned the genera among themselves. For this unique book, they have examined 4,300 strains and classified them into 39 genera and 349 species. Each species is described extensively: the macro- and microscopical appearance, the life cycle (if known), the ability to use 30 or 40 organic compounds as sole sources of carbon for aerobic growth ("assimilation"), 5 to 13 of them for semi-anaerobic "fermentation" and some additional physiological tests. The account of each species includes the number of strains examined, their sources and some information about how they vary, one from another. There is an invaluable bibliography for each chapter, and the book has a comprehensive index to the names of taxa which makes it easy to find the currently accepted synonym for almost any yeast. There is no general index.

I propose to discuss the book principally as one using it for identifying yeasts, and not to review the detailed classification. The accepted primary division of yeasts is into those that do and those that do not form ascospores. In his chapter on methods, Walt says "In view of the importance of ascospore formation as a taxonomic criterion, a strain may only be regarded as anascosporogenous when (a) it has failed to yield ascospores on a wide variety of media; (b) it has been shown not to be a haploid mating type of some or other heterothallic species." Walt lists fourteen ascogenic media. When one is faced with hundreds of strains to identify, using even half these media may be a formidable task; after inoculation they must be examined with the oil immersion objective at three days and then weekly "for at least 4–6 weeks", unless ascospores have been seen. Even after this, a negative result is equivocal. Recently, a colleague and I isolated and identified nearly 1,000 yeasts; as over 800 were (anascosporogenous) *Cryptococci*, it would have been futile to have tested them for ascospore formation.

Although ascospore formation is import-

ant in classification, formation of ascospores need not be made important in identification. An alternative to Lodder's identification key could be based primarily on growth and fermentation tests. Microscopical appearance, and even ascospore formation, could then be used for confirmation of identity and for distinguishing between species with the same responses to the physiological tests.

The nutritional tests must, of course, be uniformly carried out. On this Lodder is sanguine: "With certain minor exceptions . . . identical methods were used for every standard description, so that the individuality of each observer should not have significant effects on the results of the tests." Nevertheless, Walt refers to several methods that can be used. Though he evidently favours unshaken tubes of liquid media for growth tests, I found no statement that these were used by all the authors. The exact method of testing may not affect results when the yeast grows either well or not at all; but, even when aeration is not a limiting factor, the utilization of many test compounds often involves lags of up to several days (not a consequence of selection) and doubling times of as long as twenty hours. Such slow responses are particularly sensitive to test conditions. Hence the reaction of a given strain to one substrate may be described by different authors as positive, slow, weak or even negative. Accordingly, a new key derived from this book might use three categories of test response: positive, negative and query; the last would include all equivocal responses and those varying between strains of one species.

Compared with the first edition, written by Lodder and Kreger-van Rij and published in 1952, more than three times as many strains have been classified into over twice the number of species. The number of physiological tests has been increased from 15 to between 40 and 60, depending on the genus. The description of each species in the first edition included excellent drawings which greatly help identification; unfortunately in the second edition a number of species are illustrated sparsely or not at all.

Although the book is unwieldy, it is convenient as a single volume. Its high price will stop many buying their own copies, but the amount of information justifies the cost to any laboratory concerned with yeasts. The wealth of information about the capacities of all known kinds of yeast to utilize many organic substrates, combined with the summaries of the life cycles, is potentially of great industrial interest. It could also be an important basis for much research in microbial physiology and genetics.

JAMES A. BARNETT

CORRESPONDENCE

PhD Theses

SIR,—Every university library in the country contains scores of PhD theses, each representing three years of full-time research financed by government or industry and three years' supervision by a member of the university staff as well as accessory technical assistance and consumable equipment. The return for the several thousands spent per PhD is a thesis on the library shelf and a piece of paper for the candidate which ensures that he will command a higher salary than he could otherwise expect.

This seems unnecessarily and excessively expensive in view of the fact that although these theses are theoretically available for consultation, the difficulties encountered in attempting to refer to them verge on the insurmountable, and the scientific community thus does not benefit from the work.

An essential part of training in research should be preparation for publication, yet the PhD candidate is allowed to indulge in a verbose expansiveness that no editor of a scientific journal would contemplate for a moment.

PhD theses should consist of work written up in the form of papers which, if they are not already published, should at least have been accepted by a reputable journal. (As is the practice with certain

learned societies, the raw data on which conclusions are based may be deposited in suitable archives.) In this way a return for the large financial outlay will be guaranteed and the candidates will be trained to conduct research realistically. Furthermore, examiners will no longer be obliged to spend hours plodding through inordinate reams of rubbish to extract the few kernels of new and useful information.

My own students write directly for publication, which not only spurs their efforts during the research but saves them from the trauma of "writing up" during their last few months in the department. At the end of this, the idea of going through the thesis extracting the publishable parts and rewriting them for publication is so abhorrent that in most cases it is never accomplished.

Although in many universities it is possible to present papers alone for a PhD, there is resistance to this from both academic and administrative staff. Yet in a situation where two equally qualified applicants for a post have both submitted for a PhD—applicant A a normal thesis, applicant B papers—there is little doubt that B will be selected.

On the grounds of cost-effectiveness, obligation to the scientific community and self-interest of the candidate, the present system of preparing PhD theses

should be discarded at the earliest opportunity.

Yours faithfully,

L. BEVERLY HALSTEAD

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Dowsing

SIR,—The current (January) number of *Theoria to Theory* contains an interview with Colonel Merrylees, a past president of the British Society of Dowsters, in which he talks among other things about his selection of young men for sensitivity in dowsing at an army establishment. This work has been the subject of destructive criticism in an article in *Nature* (229, 163; 1971). A comment on the attack in *Nature* will be published in the ensuing number of *Theoria to Theory* (April).

Yours faithfully,

DOROTHY EMMET

*Editor,
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9 Marion Close,
Cambridge*

Obituary

Professor A. Ghigi

ALESSANDRO GHIGI, professor emeritus of the University of Bologna, who died in Bologna on November 20, 1970, in his ninety-sixth year, was born in that city in 1875. He was held in very high esteem in Italy, and was a member of the Pontificia Accademia delle Scienze and the Accademia Nazionale dei Lincei and also of the Accademia delle Scienze of Bologna, Torini and Modena, and many scientific societies in other countries. He was awarded honorary doctorates at the Universities of Boston and Coimbra.

His long and distinguished career encompassed many aspects of zoology; from 1902 to 1915 he was lecturer in zoology and agricultural entomology in the School of Agriculture of the University of Bologna, and subsequently lecturer in zoology and comparative anatomy in the University of Ferrara from 1904 till

1908, when he became professor, a position he held until the end of 1922. That year he was appointed to the chair of zoology at the University of Bologna, where he became Rector in 1930, a position he held for the unprecedented period of thirteen years. He directed the Institute of Zoology of the University which he established for almost thirty years, and which attained a high reputation both for its scientific and teaching standards.

He laid the basis of practical aviculture in Italy, which previously had been completely neglected, and also founded the Institute of Aviculture in Bologna. He was very interested in these subjects, and became Honorary President of the World Poultry Science Association. He was also a leading authority on ornamental pheasants and guinea-fowl. He studied the problems of game animals in relation to hunting, and contributed much biological information by the

institution of observations on migration and the establishment of a laboratory of applied zoology concerning game animals, including birds.

Ghigi made several zoological expeditions: to Cyrenaica in 1920; the Dodecanese Islands in 1926; Tehuantepec, Mexico, in 1927; Morocco in 1930; and Lake Chapala and Patzcuaro, Mexico, in 1932; on which he collected numerous species, several new to science. His publications, of which there are more than 350, cover a wide range of subjects on various aspects of zoology including morphology, genetics and systematics, and deal with mollusca, crustacea, insects, mammals and especially birds.

He made a great contribution to the conservation of wild life, both nationally and internationally, and undoubtedly did more than any single individual to secure a better preservation of wild birds in Italy. He was a vice-president of the International Council for Bird

Preservation from 1954–1966, and chairman of the Italian National Section for thirty-five years, only relinquishing this position in 1970 on account of ill health, when he was immediately elected honorary president of the section.

Ghigi was a great traveller until just before he died, and attended many international conferences. In 1968, at the age of 94, he attended a conference in Venezuela in March, followed by another in Hungary in May, and a third in Rumania in June. Ghigi was an outstanding personality wherever he went, and he will be mourned all over the world.

Academician A. I. Mikoyan

ACADEMICIAN Artem Ivanovich Mikoyan, one of the leading aircraft designers of the Soviet Union, died on December 9, 1970.

Mikoyan was born in 1905, in the village of Sanain, in Armenia. He was educated at the Zhukovskii Air Force Engineering Academy. In 1937 he became head of the design department of the experimental aircraft design bureau, and subsequently rose to be chief designer and director. In 1945, he visited Germany to study German aircraft construction methods. He was elected to the Academy of Sciences as a Corresponding Member in 1953. Together with M. I. Gurevich, he designed the series of MiG fighter aircraft. His first design for a turbojet aircraft was completed in 1946. From 1954 onwards he designed numerous types of supersonic aircraft.

For his services to the aircraft industry, Mikoyan received three Stalin Prizes (now State Prizes), one Lenin Prize, the Order of Lenin (5 times), four other Orders and a number of medals. He was twice nominated as a Hero of Socialist Labour.

The council of the **Geological Society of London** has announced the following medal awards for 1971: **Wollaston Medal**, to **Brigadier R. A. Bagnold**, for his contributions to the science of sand movement and its application to sedimentology and engineering problems; **Murchison Medal**, to **Professor B. C. King**, for his contributions to petrology and African geology; **Lyell Medal**, to **Professor P. Allen**, for his work in sedimentology; **Bigsby Medal**, to **Dr F. J. Vine**, for his contributions to the understanding of the evolution of the ocean floor. The proceeds of the Murchison Fund have been awarded to **Dr J. Dewey**, for his contributions to the understanding of the Lower Palaeozoic of the North Atlantic Province. Moieties of the Lyell Fund have been awarded to **Dr G. Evans**, for his work on recent coastal sedimentation, to **Dr J. M. Hancock**, for his work on the Cretaceous rocks of the British Isles, and to **Mr T. R. Owen**, in recognition of his services in the teaching of geology.

The recipients of the **1970 National Medal of Science**, awarded by the US Government for distinguished achievement in science, have been announced: **Professor R. D. Brauer**, Harvard University; **Professor Robert H. Dicke**, Princeton University; **Barbara McClintock**, Carnegie Institution of Washington; **George E. Mueller**, General Dynamics Corporation; **Albert B. Sabin**, Weizmann Institute of Science, Rehovoth; **Allan R. Sandage**, Carnegie Institution of Washington; **Professor John C. Slater**, University of Florida; **Professor John A. Wheeler**, Princeton University; and the late **Professor Saul Winstein**, University of California

British Diary

Monday, February 22

Concorde (6.30 p.m.) Mr B. Trubshaw, Institution of Electrical Engineers, London Graduate and Student Section, jointly with I.Mech.E., at 1 Birdcage Walk, London SW1.

Semiconductor Nuclear Devices (2.30 p.m. colloquium) Institution of Electrical Engineers, at Savoy Place, London WC2.

Tuesday, February 23

Cable Installations Designed by Computer Techniques (5.30 p.m. discussion) Institution of Electrical Engineers, at Savoy Place, London WC2.

Experiences with Electrostatic and Mechanical Dust Collectors (6 p.m. discussion) Institution of Mechanical Engineers, at 1 Birdcage Walk, London SW1.

Faraday and the Beginning of Useful Electricity (3 p.m.) Professor R. King, Royal Institution, at 21 Albemarle Street, London W1. (Lecture for Preparatory School Pupils from Schools in London and the Home Counties. To be repeated on February 24 and 25.)

Respiratory Viruses (5.30 p.m.) Dr D. A. J. Tyrrell, University of London, at the Institute of Child Health, 30 Guilford Street, London WC1. (Fourteenth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

The New Anthropology and Its Critics (5 p.m.) Mr Edwin Ardener, University of London, at the London School of Economics and Political Science, Houghton Street, London WC2. (Malinowski Memorial Lecture.)

Wednesday, February 24

Built-in Test Equipment for the Concorde (6 p.m. discussion) Institution of Electrical Engineers, at the Royal Aeronautical Society, 4 Hamilton Place, London W1.

Culpeper's Herbal: Over Three Centuries (1 p.m.) Dr F. N. L. Poynter, Royal Institution, History of Science Discussion Group, at 21 Albermarle Street, London W1.

Environment of Packages in Transit (2.30 p.m. symposium) Society of Environmental Engineers, in the Mechanical Engineering Department, Imperial College, London SW7.

Food Additive Specifications (6.15 p.m.) Dr H. Egan, Society of Chemical Industry, Food Group, at 14 Belgrave Square, London SW1.

Long Distance Waveguides (6.30 p.m.) Mr N. Lacey, Institution of Electrical Engineers, London Graduate and Student Section, at Croydon Technical College, Fairfield, Croydon, Surrey.

Announcements

University News

Professor W. Keasley Welch, University of Colorado, has been appointed Ingraham professor of neurosurgery at **Harvard University** and neurosurgeon-in-chief at the Children's Hospital Medical Center.

Appointments

Dr Kendrick W. Hare has been appointed director of the **Pakistan-SEATO Cholera Research Laboratory** in Dacca, in succession to **Dr Robert A. Phillips**.

Miscellaneous

Dr Stephen J. Smith, acting chief of the Laboratory Astrophysics Division of the US National Bureau of Standards, has been elected chairman of the **Joint Institute for Laboratory Astrophysics** for 1971 and 1972.

Dr William R. Busing, Oak Ridge National Laboratory, has been elected president of the **American Crystallographic Association** for 1971, in succession to **Dr David P. Shoemaker**, Oregon State University. **Dr Jerome Karle**, US Naval Research Laboratory, has been elected vice-president.

Professor Abdus Salam, director of the International Centre for Theoretical Physics, Trieste, and professor of theoretical physics at Imperial College, London, has been awarded the **J. Robert Oppenheimer memorial prize** of the University of Miami, in recognition of his work in quantum electrodynamics and elementary particle physics.

Muscles as Machinery (5.30 p.m.) Professor D. R. Wilkie, University of London, in the Botany Theatre, University College London, Gower Street, London WC1.

New Sources of Power for Industry (6 p.m.) Mr Arthur Palmer, MP, Royal Society of Arts, at John Adam Street, Adelphi, London WC2.

New Views on Sleep and Dreams (6.30 p.m.) Dr C. R. Evans, Institution of Electrical Engineers, at King Edward VI Grammar School, Broomfield Road, Chelmsford, Essex.

Recent Developments in Nucleonic Instruments used for Industrial Process Control (6 p.m.) Mr J. F. Cameron, Institution of Electronic and Radio Engineers, at 9 Bedford Square, London WC1.

The Determination of Trace Elements in Metallurgical Products (2.30 p.m.) Society for Analytical Chemistry, at Lanchester Polytechnic, Coventry.

Thermal Effects in Liquid Phase Reactions (2.30 p.m.) Mr W. S. Sebborn, Society for Analytical Chemistry, at the University of Essex, Colchester, Essex.

Video Recording (7 p.m.) Mr A. H. Jones, Institution of Electrical Engineers, at the Star and Garter Hotel, Dorking, Surrey.

Wind Pressure Effects on Structures (6 p.m.) Mr C. Scruton, Institution of Mechanical Engineers, at 1 Birdcage Walk, London SW1. (James Clayton Lecture.)

Thursday, February 25

Application of Micro Fragrances (7.30 p.m.) Mr R. H. Sudekum, British Society of Perfumers, at the Royal Society of Arts, John Adam Street, London WC2.

Application of the Code of Practice for the Protection of Persons Exposed to Ionizing Radiations, Mr J. M. Rees; **The Radioactive Substance Act 1960**, Mr R. G. D. Osmond; **Design of Radiochemical Laboratories in Universities**, Mr E. I. Hamilton (2.30 p.m.) Society for Analytical Chemistry, at the Wellcome Building, 183 Euston Road, London NW1.

Art and Science: 7. Abstract Art and the Sub-atomic Universe (1.30 p.m.) Mr P. D. Carpenter, University of London, at Imperial College, London SW7.

Changes and the Future in Electrical Engineering (5.30 p.m.) Mr S. Z. de Ferranti, Institution of Electrical Engineers, at the Central Hall, Westminster, London SW1. (Faraday Lecture.)

Legal Aspects of Radiochemistry (2.30 p.m.) Society for Analytical Chemistry, Radiochemical Methods Group, at the Wellcome Building, 183 Euston Road, London NW1.

Management Development in Theory and Practice (6 p.m.) Mr J. Mardon, Institution of Electronic and Radio Engineers, at 9 Bedford Square, London WC1.

Nine Delhis (5.15 p.m.) Mr Patwant Singh, Royal Society of Arts, Commonwealth Section, at John Adam Street, Adelphi, London WC2.

Node Logic (7.30 p.m.) Mr B. S. Walker, Institution of Electronic and Radio Engineers, at the J. J. Thomson Laboratory, University of Reading, Whiteknights Park, Reading.

Properties of Waves. Young and the Wave Theory of Light (1 p.m. films) Royal Institution, at 21 Albemarle Street, London W1.

Red Cells and their Enzymes (5.30 p.m.) Professor T. A. J. Pranker, University of London, at the Institute of Child Health, 30 Guilford Street, London WC1. (Last of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

Satellite Communications: Future and Trends (6.30 p.m.) Mr J. Brown, Institution of Electronic and Radio Engineers, at the University Engineering Laboratories, Trumpington Street, Cambridge.

Television Communication by Satellite and Conventional Systems (7 p.m.) Mr D. J. Whyte, Institution of Electronic and Radio Engineers, at Medway College of Technology, Chatham, Kent.

Use and Re-Use of Water in Industry (6.15 p.m. symposium) Society of Chemical Industry, Food Group, at 14 Belgrave Square, London SW1.

Friday, February 26

Effective Contraceptive Services (9 p.m.) Dr Ian A. G. MacQueen, Royal Institution, at 21 Albemarle Street, London W1. (The Woodhull Lecture.)

Laser Research at the National Physical Laboratory (1 p.m.) Mr J. W. C. Gates, Royal Institution, Photochemistry Discussion Group, at 21 Albemarle Street, London W1.

The Glass Transition Temperature of Paint Films (7.15 p.m.) Mr J. L. Prosser, Oil and Colour Chemists' Association, at the Angel Hotel, Cardiff.

Saturday, February 27

Mountain Bushmen of Eastern Lesotho—Their Art and Archaeology (3.30 p.m.) Miss Patricia Vinnicombe and Mr Patrick Carter, Inner London Education Authority, at the Horniman Museum, London Road, Forest Hill, London SE23.

Monday, March 1

How to Enjoy Food Additives (6.30 p.m.) Professor B. C. L. Weedon, Society of Chemical Industry, London Section, jointly with the Food Group, at 14 Belgrave Square, London SW1.

Telecommunications—New Practices, Old Concepts (5.30 p.m.) Professor J. Greig, Institution of Electrical Engineers, at Savoy Place, London WC2.

The Use of Computers in Aircraft (7 p.m.) Mr B. J. Calvert, Institution of Electrical Engineers, at the Royal Star Hotel, Maidstone, Kent.

Reports and Publications

not included in the monthly Books Supplement

Great Britain and Ireland

British Medical Bulletin, Vol. 27, No. 1, (January 1971): Symposium on Epidemiology of Non-Communicable Disease. Pp. 1-94. (London: British Council, 1971.) £2. [41]

The Zoological Record, 1966, Vol. 103, Section 13: Insecta. Prepared by the Commonwealth Institute of Entomology and the Zoological Society of London. Pp. xvi+417. 1968, Vol. 105, Section 4: Coelenterata. Compiled by the Staff of the Zoological Society of London. Pp. iv+39. £1. 1968, Vol. 105, Section 7: Brachiopoda. Compiled by Margaret O'Hanlon. Pp. iv+24. £1. 1968, Vol. 105, Section 8: Bryozoa (Polyzoa) and Entoprocta. Compiled by Eileen Hutton. Pp. 24. 1968, Vol. 105, Section 17: Reptilia. Compiled by David Cole. Pp. vi+74. £2. (London: The Zoological Society of London, 1970.) [41]

Yorkshire Flooding—Some Effects on Man and Nature. By J. Radley and C. Simms. Pp. 28. (York: Sessions Book Trust, The Pbor Press, 1971.) 50p. [41]

Ministry of Transport: Road Research Laboratory. RRL Report LR 369: Air-Photograph Interpretation for Road Engineers in Britain. By Dr M. J. Dumbleton and G. West. Pp. 24. (Crowthorne, Berkshire: Road Research Laboratory, 1970.) [41]

Bulletin of the British Museum (Natural History). Geology, Vol. 19, No. 6: Scottish Callovian and Oxfordian Ostracoda. By R. C. Whitley. Pp. 297-358/15 plates. £4.80. Vol. 19, No. 8: The Lower Palaeozoic Stratigraphy and Faunas of the Taurus Mountains near Beyşehir, Turkey. 1: Stratigraphy. By W. T. Dean and Ö. Monod. Pp. 411-426. 65p. Zoology, Vol. 20, No. 4: A Review of the Species of *Hemilepistus* S.Sir. Budden-Lund, 1885 (Isopoda, Porcellionidae). By R. J. Lincoln. Pp. 109-130. 80p. Vol. 21, No. 1: Decapod Crustacea Larvae collected during the International Indian Ocean Expedition. Families Raninidae and Homolidae. By A. L. Rice. Pp. 1-24. 85p. (London: British Museum (Natural History), 1970.) [41]

Fabian Tract No. 404: A Social Democratic Britain. By Anthony Crosland. Pp. 16. (London: Fabian Society, 1971.) 15p. [51]

Bulletin of the British Museum (Natural History). Geology, Vol. 19, No. 5: Two Upper Cretaceous Salmoniform Fishes from the Lebanon. By Colin Patterson. Pp. 205-296+5 plates. £3.90. Zoology, Vol. 20, No. 7: The Species of *Macrophthalmus* (Crustacea: Brachyura) in the Collections of the British Museum (Natural History). By R. S. K. Barnes. Pp. 203-251. £1.40. (London: British Museum (Natural History), 1970.) [51]

Royal Observatory Annals No. 5: Catalogue of Stars within twenty-five parsecs of the Sun. By Sir Richard Woolley, Elizabeth A. Epps, Margaret J. Penston and Susan B. Pocock. Pp. 227. (Hertsmere, Sussex: Royal Greenwich Observatory, 1970.) £4.40 net. [51]

University of Cambridge—Department of Agricultural Science and Applied Biology Memoirs. No. 42: A Summary of the papers published and research in progress by the members of the Department and its Associated Research Organizations during the period 1 October 1969-30 September 1970. Review Series No. 25: Research in Animal Nutrition, 1950-1970. Pp. 25. (Cambridge: The University, 1970.) 15p. [71]

Wildfowl 21. Edited by G. V. T. Matthews and M. A. Ogilvie. Pp. 160+16 plates. (Slimbridge, Gloucester: The Wildfowl Trust, 1970.) £1.25. [81]

De Beers Diamond Research Laboratory. Diamond Information L22: Grinding with Diamond Abrasives. Part 1—Steel. By Dr Henry B. Dyer. Pp. 15. Diamond Information L23: Grinding with Diamond Abrasives. Part 2—Tungsten Carbide. By F. Hughes. Pp. 24. (London Industrial Diamond Information Bureau, 7 Rolls Buildings, EC4, 1971.) gratis. [81]

- Nuffield Committee for the Advancement of Medicine—Annual Report 1969. (Supplement No. 1 to the *University Gazette*, Vol. ci, November 1970.) Pp. 17. (Oxford: The University, 1970.) 40p. [111]
- Building Research Station Digest, No. 125: Colourless Treatments for Masonry. Pp. 3. (London: HMSO, 1971.) 5p. [111]
- Physiological Plant Pathology*, Vol. 1, No. 1, January 1971. Pp. 1-82. Volume 2, 1971, 4 issues. Inland £7 plus £0-40 postage; Abroad \$19 plus \$0.50 postage. (London and New York: Academic Press, 1971.) [111]
- Bulletin of the British Museum (Natural History). Zoology, Vol. 20, No. 6: Observations on the Electric Dolphin, *Peponocephala electra*. By W. A. Dawbin, B. A. Noble and F. C. Fraser. Pp. 173-210. (London: British Museum (Natural History), 1970.) 90p. [131]
- BBC Handbook 1971. Pp. 272. (London: BBC, 1971.) 50p. [131]
- Women in the Factory: a Study of Job Satisfaction and Labour Turnover. By Ray Wild and Dr A. B. Hill. Pp. 96. (London: Institute of Personnel Management, 1971.) £1.50. [131]
- Ministry of Agriculture, Fisheries and Food. Technical Bulletin No. 18: Manual of Veterinary Parasitological Laboratory Techniques. Pp. vi+131 +7 plates. (London: HMSO, 1971.) 90p net. [141]
- NLL Announcement Bulletin: a Guide to British Reports, Translations and Theses, Vol. 1, No. 1, January 1971. Pp. 1-50. (Walton, Boston Spa: National Lending Library for Science and Technology, 1971.) [141]
- Universities Research Reactor—Annual Report 1969/1970. Pp. vii+29. (Warrington, Lancs: Universities Research Reactor, 1971.) [141]
- Jubilee Report of the Welsh Plant Breeding Station, 1919-1969. Pp. 236. (Pias Gogerddan, near Aberystwyth: Welsh Plant Breeding Station, 1970.) 50p. [141]
- Bulletin of the British Museum (Natural History). Geology, Vol. 19, No. 7: A Palynological Study of Two of the Neogene Plant Beds in Derbyshire. By M. C. Boulter. Pp. 359-410+9 plates. £3.10. Vol. 20, No. 1: The Lower Palaeozoic Stratigraphy and Faunas of the Taurus Mountains near Beyşehir, Turkey. II. The Trilobites of the Seydischir Formation (Ordovician). By W. T. Dean. Pp. 1-24+5 plates. £1.75. Zoology, Vol. 20, No. 5: A Taxonomic Revision of the Oligochaete Genus *Eukerria* Michaelsen 1935 (Ocnodrilinae, Megascotocidae). By Barrie Gillean Molyneux Jamieson. Pp. 131-172. £1.30. (London: British Museum (Natural History), 1970 and 1971.) [141]
- Ministry of Agriculture, Fisheries and Food—National Agricultural Advisory Service. Experimental Husbandry Farms and Experimental Horticulture Stations—Eleventh Progress Report. Pp. v+140+8 plates. (London: HMSO, 1970.) 75p. [151]
- University of Manchester Institute of Science and Technology. Annual Report 1969/1970. Pp. 101. (Manchester: UMIST, 1971.) [151]

Other Countries

- Neurosciences Research Program. Bulletin, Vol. 8, No. 4 (September 1970): Macromolecules in Synaptic Function—a Report based on an NRP Work Session. By Floyd E. Bloom, Leslie L. Iversen and Francis O. Schmitt. Pp. 325-455. (Brookline, Mass.: Neurosciences Research Program, 280 Newton Street, 1970.) \$10 (private individuals who certify that subscription is for their personal use). \$20 (libraries, research units and other multiple-readership groups). [2912]
- Unesco. Annual Summary of Information on Natural Disasters, No. 3, 1968. Pp. 72. (Paris: Unesco; London: HMSO, 1970.) 10 francs; 75p; \$2.50. [2912]
- India: National Geophysical Research Institute. Geophysics Research Board. Progress in Geophysics—Report on the Geophysical Activities in the Republic of India, No. 4, January-December, 1968. (Hyderabad: National Geophysical Research Institute, 1970. Rs. 7.50; \$1.50.) [2912]
- World Health Organization. Public Health Papers, No. 40: Principles and Practice of Cholera Control. By J. de Araoz et al. Pp. 140. (Geneva: WHO; London: HMSO, 1970.) 8 Sw. francs; 80p; \$2.75. [2912]
- Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Paper 69-52: Preliminary Notes on the Hurwitz Group. Padlei Map—Area, Northwest Territories. By R. T. Bell. Pp. vi+13. \$1.50. Map 900A: Principal Mineral Areas of Canada. Twentieth edition. (Ottawa: Queen's Printer, 1970.) [2912]
- Occasional Papers of the California Academy of Sciences. No. 82: Catalog of Specimens in the Type Collection of the Department of Geology, California Academy of Sciences. Cephalopoda. By Victor A. Zullo and Leo G. Hertlein. Pp. 130. No. 83: The Genus *Enlalia* Aldrich in America North of Mexico (Diptera: Dolichopodidae). By Harold Robinson and Paul H. Arnaud, Jr. Pp. 9. No. 84: A New Species of the Genus *Platymanis* (Ranidae) with a List of Amphibians Known from South Gigante Island, Philippines. By Walter C. Brown and Angel C. Alcalá. Pp. 8. Proceedings of the California Academy of Sciences, Fourth Series. Vol. 37, No. 13: On the Diet and Feeding Behaviour of the Northern Anchovy *Engraulis mordax* (Girard). By Anatole S. Loukashkin. Pp. 419-458. Vol. 37, No. 14: *Polydora altoporis*, New Species, a Commensal Spionid (Annelida, Polychaeta) from a Hydrocoral Off Central California. By William J. Light. Pp. 459-472. Vol. 37, No. 15: Benthic Fishes Cast Ashore by Giant Waves Near Point Joe, Monterey County, California. By W. I. Follett. Pp. 473-488. (San Francisco: California Academy of Sciences, 1970.) [3112]
- Harvard University. Program on Technology and Society. Reprint No. 9: The Function of Tort Liability in Technology Assessment. By Milton Katz. Pp. 587-662. (Cambridge, Mass.: Harvard University, 1970.) [3112]
- Renin—Angiotensin Mechanisms—a Review of Research Grants Supported by the National Heart and Lung Institute, 1949 to 1970. By May Sherman. Pp. vi+140. (Bethesda, Md.: National Institutes of Health—Extramural Research and Training, 1970.) [3112]
- Bulletin of the American Museum of Natural History. Vol. 143, Article 3: Breeding Tubercles and Contact Organs in Fishes—Their Occurrence, Structure and Significance. By Martin L. Wiley and Bruce B. Collette. Pp. 143-216. (New York: American Museum of Natural History, 1970.) \$2.25. [3112]
- International Union for Conservation of Nature and Natural Resources. IUCN Eleventh Technical Meeting, New Delhi, India, 25-28 November 1969. (IUCN Publications, New Series No. 17.) Pp. 282. (Morges, Switzerland: IUCN, 1970.) [41]
- Studia Forestalia Suecica. Nr. 83: Mycorrhiza and Tree Nutrition in Poor Forest Soils. By Erik Björkman. Pp. 24. Nr. 84: Biological Control of *Fomes annosus* in Norway Spruce (*Picea abies*) with Immunizing Commensals. By J. L. Ricard. Pp. 50. 15 kr. Nr. 85: Low-Temperature Induced Irregularities in Pollen Mother Cells of *Larix leptolepis*. By Gösta Eriksson. Pp. 14. 5 kr. Nr. 86: Photo- and Thermoperiodic Responses of Different Larch Provenances (*Larix decidua* Mill.) By Milan Simak. Pp. 31. 9 kr. Nr. 87: Further Studies on Meiosis and Pollen Formation in *Larix*. By Gösta Eriksson, Inger Ekberg and Alena Jonsson. Pp. 65. 17 kr. Nr. 88: Plant Condition and Plant Growth—Planting Experiments with Spruce (*Picea abies* (L.) Karst.) on Calluna Heath Land. By Erik Björkman. Pp. 36. 9 kr. (Stockholm: Skogshögskolan, Royal College of Forestry, 1970.) [41]
- Bulletin of the American Museum of Natural History. Vol. 143, Article 1: The Genus *Sarothra* (Aves, Rallidae). By Stuart Keith, C. W. Benson

- and M. P. Stuart Irwin. Pp. 1-84. (New York: American Museum of Natural History, 1970.) \$3.50. [51]
- US Department of the Interior: Geological Survey. Water-Supply Paper 1984: Hydrologic Effects of Floodwater-Retarding Structures on Garza-Little Elm Reservoir, Texas. By C. R. Gilbert and S. P. Sauer. Pp. vii+95+3 plates. (Washington, DC: Government Printing Office, 1970.) [61]
- Smithsonian Contributions to Zoology, No. 60: Studies of Neotropical Caddisflies, 10: Leucotrichia and Related Genera from North and Central America (Trichoptera: Hydroptilidae). By Oliver S. Flint, Jr. Pp. 64. (Washington, DC: Smithsonian Institution Press, 1970. For sale by US Government Printing Office.) \$1.25. [61]
- Republic of South Africa. Department of Industries: Division of Sea Fisheries Investigational Reports. No. 84: Notes on an Oxygen-Depleted Subsurface Current Off the West Coast of South Africa. By A. H. B. De Decker. Pp. 24. No. 88: Marine Algae from Southern Africa. 1: Six New Species from the Inter- and Infra-Tidal Zones. By K. H. Simons. Pp. 13. (Sea Point, Cape Town: Division of Sea Fisheries, 1970.) [61]
- Fisheries Research Board of Canada. Technical Reports. No. 202: Utilisation des Diatomées Benthiques comme Indicateur de Pollutions Minérales dans le Bassin de la Miramichi N. W. Par W. K. Besch, M. Ricard et R. Contin. Pp. 72. No. 204: Tag Recaptures and Movements of Adult Male Snow Crabs *Chionoecetes opilio* (O. Fabricius) in the Gaspé Region of the Gulf of St. Lawrence. By J. Watson. Pp. 11. (St. Andrews, NB: Fisheries Research Board of Canada, Biological Station, 1970.) [61]
- International Union for Conservation of Nature and Natural Resources. IUCN Eleventh Technical Meeting, New Delhi, India, 25-28 November 1969, Papers and Proceedings, Vol. 2. (Morges: Switzerland, IUCN, 1970.) [71]
- Cancer in Crisis. Pp. 72. (New York: Memorial Sloan-Kettering Cancer Center, 1970.) [81]
- US Department of the Interior: Geological Survey. Bulletin 1284: Paleozoic Stratigraphy in the Northwest Coastal Area of Prince of Wales Island, South-eastern Alaska. By G. C. Eberlein and Michael Churkin, Jr. Pp. iv+67+2 plates. \$0.65. Bulletin 1294-B: Probable Permian Age of the Rampart Group, Central Alaska. By W. P. Brosge, M. A. Lanphere, H. N. Reiser, and R. M. Chapman. Pp. iii+18. \$0.20. Bulletin 1312-H: Geology, Mineral Deposits and Geochemical and Radiometric Anomalies, Serpentine Hot Springs Area, Seward Peninsula, Alaska. By C. L. Sainsbury, T. Hudson, R. Kachadoorian and Thomas Richards. Pp. iii+19+plate 1. Water-Supply Paper 1608-K: Water Resources and Related Geology of Dera Ismail Khan District, West Pakistan, with reference to the Availability of Ground Water for Development. By James W. Hood, Lutfi Ali Khan and K. Jawaid. Pp. viii+74+6 plates. Water-Supply Paper 1879-G: Dispersal of Plating Wastes and Sewage Contaminants on Ground Water and Surface Water, South Farmingdale-Massapequa Area, Nassau County, New York. By N. M. Perlmuter and Maxim Lieber. Pp. v+67+5 plates. Water-Supply Paper 1891: Geohydrology of Finney County, Southwestern Kansas. By Walter R. Meyer, Edwin D. Gutentag and David H. Lohmeyer. Pp. vii+117 +2 plates. (Washington, DC: Government Printing Office, 1970.) [111]
- World Health Organization. European Standards for Drinking Water. Second edition. Pp. 58. (Geneva: WHO; London: HMSO, 1970.) 4 Sw. francs; 40p. [111]
- US Department of Agriculture: Agricultural Research Service. Miscellaneous Publication No. 1178: The Potential for Genetic Suppression of Insect Populations for their Adaptations to Climate. By W. Klassen, J. F. Crech and R. A. Bell. Pp. 77. (Washington, DC: Government Printing Office, 1970.) \$0.60. [111]

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